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COMPARATIVE STUDY OF MAJOR CONGENITAL BIRTH DEFECTS IN CHILDREN OF 0-2 YEARS OF AGE IN THE GAZA STRIP, PALESTINE

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ABSTRACT

In the Gaza strip, congenital malformations are the first leading cause of infant deaths. The present study aims to collect and evaluate the available recorded information about the occurrence of major birth defects (BD) in the Gaza Strip in patients between 0 and 2 years of age and compare this between the two periods under review, the first 6 months 2006 and the corresponding six months in 2010. We collected the records of children between 0 and 2 years admitted with major structural birth defects (BD) in the major pediatric hospitals of the Gaza Strip. The frequency of BD in the age group 0-2 year was higher in 2010 (63/1000 hospital admission) than 2006 (39.5/1000). The estimated prevalence of major BD jumped from 5.83 in 2006 to 6.76 in 2010. Congenital heart diseases (CHD) are the most common reported BD in both times and there is marked increase in both Renal and Neural tube defects in 2010. Improving BD registry and further investigation of environmental factors are recommended.

INTRODUCTION

In the Gaza strip, congenital malformations are the first leading cause of infant deaths. The year 2003 statistics show that 14.3% of newborn with congenital malformation do not survive (West Bank 12.1% and 15.8% in Gaza Strip) and that the specific infant mortality due to congenital anomalies increased in time from 0.2 % in 1995 to 0.38 % in 2003 (MOH, 2012). Increase in the presentation of birth defects and infant and child cancer are reported from local professionals active in war-ridden territories, in general in absence of solid numbers, and based on experiential observation, because of absence of previous registration systems in their country, and often of reduced resources and personnel (Amy *et al*., 2010). Uranium, and its isotope DU, were extensively used in bullets and bombs. Highly destructive weapons of war (small smart bombs, thermo baric grenades and shape charged weapons) have been "enhanced" by powered carcinogenic and teratogenic metals, and "not fragmentation" devices use particulate and potentially toxic metals (Apperson *et al*., 2007). Weaponry of these kind, of US and Israeli production, has been utilized extensively in Iraq, Afghanistan, Lebanon and Gaza. In Gaza toxic and carcinogenic metals were detected in craters and as components of the WP ammunition (Thiokol Aerospace, US) (New weapons 2010[a]) in the wounds produced by "not fragmentation weapons" and in the burns caused by WP (Skaik *et al*., 2010), and were still detected at a distance of 1 year from the attacks of Cast Lead in the hair of children, sign of their persistence in the environment (New weapons 2010[b]). Metals in particulate and powder forms can enter the human body via all routes of exposure including inhalation, ingestion, and skin contact for some of them. Some metals, like mercury, aluminum and molybdenum, can reach the placenta even after just dermal adsorption. Many metals present in weaponry can induce pathologies, cancers and birth defects; through multiple mechanisms of action (New weapons 2010[b], Hassan *et al*., 2010, Pereira, 2004). Exposure to metals leads to accumulation in the body where they persist as a long term burden with potential effects on health. Association between specific metal load and a pathology has been shown in environmental surveys of populations (Hassan *et al*., 2010, Pereira, 2004), and animal experiments have established cause-relationship effects between metal load and pathologies, genetic and major functional alterations, for example

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teratogenic or carcinogenetic effects (Gilani *et al*., 1990, Domingo *et al*., 1989). Toxicological, epidemiological and animal studies have established that excess of metals can disrupt body functions and have pathogenic effects in human respiratory organs, kidney and skin and affect sexual and neurological development and function. Exposure to metals of the developing fetus cause birth defects in animal studies (Gilani *et al*., 1990, Domingo *et al*., 1989). In Gaza, in utero exposure to high mercury levels is associated with birth defects and mother's documented exposure to weapons in Cast lead (Manduca *et al*., 2014)

Background

The Gaza Strip is an elongated area that stretches along the Mediterranean Sea. The length of the Gaza Strip, from Rafah in the South to Beit Hanoun in the North, measures 50 Kilometers. Its width reaches 5-7 Kilometers in the northern section to a maximum of 12 Kilometers in the Southern area with an area of 365 square kilometers and altitude of 0-40 meters above sea level. In 2010 the Gaza Strip population was estimated to be around 1.5 Million. Population growth is about 5%, fertility is about 6, and the birth rate is 37.1% per 1000 population (MOH, 2012). The total refugee population consists 65% of the general population. About 55.1% of them live in crowded camps and the remaining 44.9% live outside the camps in villages and towns. The Gaza Strip is divided into five Governorates: North, Gaza, Mid-zone, Khan Younis, and Rafah. Eighteen per cent of the population resides in North, 37 % resides in Gaza, 14 % reside in the Mid-zone, 19 % reside in Khan Younis, and 12 % in Rafah. There are three types of residential localities in the Gaza Strip: rural (villages), camps, and towns, with different crowding and level of services and hygienic facilities. In total there are 8 refugee camps, 14 villages, and 4 towns. Around 53% live in urban areas (towns), and 35% live in refugee camps.

The secondary health care services is mainly run by the Ministry of Health (MoH), children are assisted in three pediatric governmental hospitals, Nasser pediatric, Dora Pediatric and Rantisi Specialized Pediatric Hospital, and one general Hospital, European. We retrieved the data presented here in all four Hospitals. In addition, a major private Obstetric and Gynecological hospital, Emiraty Hospital has a children section and was also included in the study. In the Gaza Strip, a project in 2011 (Naim *et al*., 2012) showed that there is no systematic registry of newborn children, the diagnosis of BD in the maternity Hospitals was in most cases only clinical, and the children with clear or suspected BD are often dispatched directly to pediatric hospitals or for surgery. The Pediatric hospitals have means for objective and instrumental diagnosis and have recently developed a consistent system of registration and collection of patient information.

Purpose of the study

The present study collected and evaluated the information recorded in the Pediatric hospitals about the occurrence of major birth defects (BD) in the whole of Gaza Strip in patients between 0 and 2 years of age. We aimed to compare the prevalence in two periods: the first 6 months 2006 and the corresponding six months in 2010. We present a comparison of the frequencies of occurrence of 11 classes of birth defects in each of these periods of time, and describe their distribution in the territory. We use as base line the total number of children between 0-2 years registered in the same period of time in the Hospitals which participated to the study.

Study objectives

- To estimate the frequency of major BD among children registered in Pediatrics between 0 and 2 years of age in the Gaza Strip. To investigate potential localized conditions/ factors related to the occurrence of BD in the population under study.
- To offer initial information about the need to support unified registration procedure in Pediatric Hospitals, upgrading of the existing cytogenetic and postnatal diagnostic services in Gaza, and establishment of a Registry of congenital anomalies.
- To provide preliminary data and establish a frame for investigation of the risks from environmental exposure to war events on maternal-infant health in order to take future preventive actions.

MATERIALS AND METHODS

The study was cross sectional comparative study; we reviewed retrospectively medical records of all children between 0 and 2 year of age admitted in all pediatric hospitals of the Gaza strip during the first six months of 2006 and in the first six months of 2010. Demographic details, associated risk factors and the type of congenital anomalies in babies were recorded. Diagnosis of congenital anomalies was based on clinical evaluation of newborn by experienced neonatologist. Data were collected by trained physicians from all five pediatric hospitals in Gaza strip (Nasser, Dorah, Rantesi, European and Emiraty). The records of patients between 0 and 2 years admitted during the first six months of 2006 and 2010 with diagnosis of congenital anomaly were selected and transferred to an abstract sheet, prepared for the purpose.

Statistical Analysis

The data were introduced using SPSS (Statistical Package for Social Science version 20.0) program. Data cleaning was completed by checking for entry errors using a frequencies and logical checks on all variables. Data analysis was carried as follows: Descriptive analysis for all the study variables to examine the distribution of different factors among the population examined in the study. International classification of Diseases (ICD – 10) was used to classify major BD. Frequencies of major BD were calculated on the total admitted children of the age range 0-2 years and on that of all hospital admissions (0 – 12 Year). Frequencies of major BD in different residence areas in 2006 and 2010 were compared using Chi square test for measuring statistical differenced between proportions. Epi info stat calculator was used to calculate Chi square and P value less than 0.05 is considered statistical significant.

RESULTS

Table 1 illustrates that the total number of patients aged 0-2 years registered during 2006 were 6920, and 274 of these had diagnosis of birth defect (BD). During 2010 total of 5254 children were admitted to the hospitals, 331 with a diagnosis of birth defect. The frequency of BD in the age group 0-2 year in 2010 (63/1000 hospital admission) was significantly higher than 2006 (39.5/1000) if referred to the children of the same age range admitted. An estimate on the basis of number of total births equally shows significant differences between the years 2006 and 2010. Table 2 shows that the distribution of birth defect by gender occurs with a male to female ratio of 1.16:1 in 2006 and of 1.43:1 in 2010, without significant differences in the sex distribution between the years. Not in all cases the familiarity of the parents was found in the records.

Table 1. Prevalence and Frequency of Major birth defects per 1000 admission in all hospitals in the first six months of 2006 and 2010

First 6 months of year	2006	2010	P value
BD patients (during 6 months)	274	331	<0.001
Total 0-2 year old patients	6920	5254	
Frequency of BD (0 -2 years old)	39.6/1000	63/1000	
Estimated BD /year	548	662	
Children born in the biennias considered	93,760	98,064	
Minimal estimated prevalence Per 1000 children	5.83	6.76	<0.001

Among those recorded in 2006, 14 in 27 (46.6%) had parents first cousins and 13 (43.3%) had related parents. In 2010, among 139 recorded, 41(29.5 %) had first cousin parents and 45 (32.4%) had related parents. The frequency of baby with birth defect with unrelated parents increased significantly (P value 0.01) from 10% in 2006 to 38.1% in 2010. In 2006, 44.9% BD patients were children of families' resident in the camps of the Gaza Strip; in 2010, 54.7% of them were residents in towns. The differences between occurrence of birth defects in different kind of dwelling is highly statistically significant (P value = 0.001). Table 3 shows the distribution of the residence by governorates of the infants diagnosed with birth defects. The highest percent of cases were observed both in 2006 and 2010 in residents of the Gaza governorate, respectively 36.1% in 2006 and 41.1% in 2010. The difference between 2006 and 2010 in North and Middle zone governorates was not significant, while were significant the decrease in KanYounes and the increase in Gaza and Rafah governorates: the increase in these last governorates thus account for the overall increase between year 2006 and 2010. The data point to the relevance of local changes that have occurred in environmental conditions in the different Governorates between the year 2006 and 2010.

Table 2. Characteristics of the reported Birth defect children, in the first semester of 2006 and of 2010

		2006		2010		P value
		Number	Percent	Number	Percent	
1. Sex	Male	147	53.6	195	58.9	= 0.19
	Female	127	46.4	136	41.1	
	Total	274		331		
2. Consanguinity*	1st Degree	14	46.7	41	29.5	= 0.01
	2nd Degree	13	43.3	45	32.4	
	Not	3	10	53	38.1	
3.Kind of dwelling	Town	105	38.3	181	54.7	< 0.001
	Refugee camp	123	44.9	117	35.3	
	Village	46	16.8	33	10	

**data on familiarity were not always recorded at the time of hospitalization*

Table 3. Estimated Prevalence of Major Birth Defects by locality of residence

Locality	North	Gaza	Middle Zone	Khan-younis	Rafah	Total
Number of BD (6 months) 2006	61	99	49	41	24	274
Estimated BD (12months) 2006	122	198	98	82	48	548
Estimated % 0 – 2 years old children 2006	16,314	35,490	12,870	17,560	11,526	93,760
Estimated Prevalence Per 1000 (2006)	7.41	5.52	7.61	4.66	3.80	5.83
P value for locality differences (2006)				<0.001		
Number of BD (6 months) 2010	70	136	47	30	48	331
Estimated BD (12months) 2010	140	272	94	60	96	662
Estimated % 0 – 2 years old children 2010	16,484	35,816	13,612	19,512	12,640	98,064
Estimated Prevalence Per 1000 (2010)	8.50	7.60	6.90	3.08	7.60	6.76
P value for locality differences (2010)				<0.001		
P value for differences between 2006 and 2010 in each Governorate	0.3	<0.001	0.4	0.01	<0.001	

Table 4. Distribution of birth defect according ICD10 classification by year

	2006			2010			P Value
	Number	Percent	Frequency/1000	Number	Percent	Frequency/1000	
Congenital Heart Disease	207	75.5	29.9	189	57.7	27.3	0.07
Cleft palate & Cleft Lip	1	0.4	0.1	2	0.6	0.3	
Neural tube defects (NTD)	1	0.4	0.1	19	5.7	2.7	<0.001
Limb defects	7	2.6	1.0	7	2.1	1.0	
Skeletal Anomalies	4	1.5	0.6	1	0.3	0.1	
Genital Anomalies	6	2.2	0.9	2	0.6	0.3	
Gastrointestinal Anomalies	24	8.8	3.5	28	8.5	4.0	0.120
Renal Anomalies	6	2.2	0.9	49	14.8	7.1	<0.001
Down syndrome	9	3.3	1.3	10	3	1.4	0.404
Osteogenesis imperfecta	1	0.4	0.1	3	0.9	0.4	
others	8	2.9	1.2	21	6.3	3.0	

Table 4 shows the different types of birth defects classified according to ICD-10: cardiovascular defects (CHD) were the most common both in 2006 (29.9/1000 admission) and in 2010 (27.3/1000 admission) without significant difference between the years (P = 0.07). The gastrointestinal anomalies were the second most frequent cases in both years and no significantly different between years (P = 0.120). Renal anomalies and neural tube anomalies were significantly different between the two years, respectively for renal defects from 2.2% to 14.8%, and for neural tube defects from 0.4% to 5.7%. These changes thus account for most of the increase detected in birth defects frequency between 2006 and 2010in in both cases the differences are highly statistical significant (P < 0.001).

DISCUSSION

We here report that the frequency of major structural birth defects among hospitalized patients under 2 years of age in the first semester of 2010 was 65/1000, showing a highly significant increase compared to 39.5/1000in the corresponding period of 2006. We also report that this increase is mostly due to increase in prevalence of Neural tube and Renal defects, that it occurs prevalently in families with not consanguineous parents, town dwellers in the governorates of Gaza and Rafah. The prevalence of BD, already in 2006, is higher in Gaza compared to not highly industrialized areas of the same ethnicity. Incidence is 9.3/1000 of total births in the Libyan Arab Jamahiriya (Singh *et al*., 2000), 7.2/1000 of total births in Bahrain, 8.5/1000 of live births in Saudi Arabia and 12.5/1000 in United Arab Emirates (Arrayed, 1987, Magbool *et al*., 1989). In more industrialized south Tehran, Iran, the prevalence of congenital anomalies is 23/1000 (Tootoonchi, 2003) and is 31.7/1000in Egypt (Temtamy *et al*., 1998). Similar to what reported in neighboring countriesthe majority of BD affected children was male, both in 2006 and 2010. The distribution of the types of birth defects shows Congenital Heart Disease as the most common BD, both in 2006 and 2010, consistent with results from studies in UAE, Saudi Arabia and Kuwait (Arrayed, 1987, Magbool *et al*., 1989, March of Dimes, 2012).

Known monogenic BD as O.I, as well as chromosomal defects as Down syndrome, also included in the study, did not present a significant change in incidence in the two periods. Neural tube defects, and Renal anomalies, malformations known to be induced by environmental stressor had significantly higher prevalence in 2010 compared to 2006. A role of environmental induction of these birth defects is coherent with the fact that parents of affected children were less often first degree kin in 2010 than in 2006. The increase we detect here is also in agreement with the observation, previously reported, that a continuous increase of BD prevalence in Gaza started in 2005 and was ongoing in 2010, that these birth defects occurred sporadically and in couples without previous family history of the defect (Naim *et al*., 2013). The distribution per area of the strip shows that the increase of BD observed in 2010 occurs in the urban areas of Gaza and Rafah governorates. In speculating on which environmental changes may have occurred from 2006 to induce increase of BD in these areas, is outstanding that these were subjected to particularly heavy bombing during attacks of Cast Lead. Since exposure to weaponry was shown to be correlated with significantly higher incidence of birth defects (Naim *et al*., 2012) and corresponded to in utero contamination of the newborns with teratogen war remnants (Manduca *et al*., 2014), this is a likely reason for the increase in prevalence observed in this study. Another likely effector could be in the materials consequent to rubble removal of bombed buildings and in those derived from the recycling in open air of the debris from these. Less important should be the contamination by pesticides and insecticides, given that the increase in BD is detected mostly in urban areas, while the pollution by traffic, Diesel electrical generators and solid waste burning, should be of less impact in the smaller towns of North and Rafah that in the more extended urbanized area of Gaza city. Nonetheless, we cannot point decisively to one factor and exclude that other unknown factors may have a role, because of limited collection of environmental exposures data of the parents of these children during the registration of the patients. Limits of the study: This study includes patients admitted in the Hospitals in Gaza and does not account for perinatal deaths and patients transferred for treatment abroad. The modality of registration of incoming patients did not account for environmental exposures of the parents or their reproductive history and residential history. We recommend establishment of registration at birth (Romitti, 2007) that includes a sound neonatologist ascertainment of the health of the neonates and a thorough collection of family reproductive history, residential and work history and environmental exposures of the parents.

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