Incidence, types, geographical distribution, and risk factors of congenital anomalies in Al-Ramadi Maternity and Children's Teaching Hospital, Western Iraq

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ABSTRACT

الأهداف: دراسة معدل حدوث وأنواع والتوزيع الجغرافي وعوامل الخطورة المسببة للتشوهات الخلقية الولادية في مستشفى النسائية والاطفال التعليمي، مدينه الرمادي، غرب العراق.

الطريقة: تمت دراسة 5864 طفل حديثي الولادة خلال الفترة من شهر اكتوبر 2010م إلى اكتوبر 2011م في مستشفى الرمادي للنسائية والأطفال للفحص عن التشوهات الخلقية عند الولادة. المعلومات التي تم جمعها شملت اسم الطفل، وجنسه، ووزنه، ونوع التشوه الخلقي، وعمر الأم، ومكان السكن، والتحصيل الدراسي، وعدد الولادات السابقة، وصله القربى من الزوج، والتعرض للتدخين عند الحمل، والأمراض والأدوية المتناولة عند الحمل وتاريخ مراجعه مراكز الرعاية الصحية، ونتيجة فحص السونار قبل الولادة، وعمر الأب، وفيما إذا كان مدخناً، ووجود تشوه خلقي آخر في أحد أفراد العائلة أو الأقارب. مقابل كل طفل مصاب بالتشوه الولادي تم اختيار طفلين غير مصابين للمقارنة وتم جمع نفس المعلومات عنهما. جرى تصنيف أنواع ومعدل انتشار التشوهات التي تم اكتشافها وتم حساب معدل نسبه اود لتقييم عوامل الخطورة المؤدية لتلك التشوهات الخلقيه.

النتائج: المعدل الإجمالي لحدوث التشوهات الخلقية كان 40.5/1000، للولادات الحيه 40.8/1000 وللولادات الميتة 270.0/1000 . حوالي 20% من التشوهات الخلقية وجدت بشكل تشوهات متعددة و 80% بشكل تشوهات منفردة، و 63.8% من التشوهات كانت تشوهات كبيره وخطيرة و 36.2% تشوهات صغيره وغير مؤثره على حياه الإنسان. تشوهات جهاز القلب والأوعيه الدموية كانت الأكثر انتشاراً يليها جهاز المسالك البولية والتناسلية. العوامل المؤثرة المعنوية المرافقة لحدوث التشوهات الخلقية هي الطفل الذكر، وذو الوزن أقل من 2500 غم، والتدخين عند الأم، ووجود تشوه ولادي آخر عند العائلة، ووجود صله قربى مع الزوج، والزيادة في عدد الولادات، والزيادة أو القلة في السائل الامنيوني عند الحمل أو وجود تشوه ولادي بتشخيص السونار قبل الولادة كانت عوامل مؤثره معنوية مرافقه أو لها صله في حدوث التشوهات الخلقية، بينما عمر الوالدين، والمستوى الدراسي للأم هي عوامل غير مؤثره.

خاتمة: رغم أن معدل حدوث التشوهات الولاديه وجدت أقل من تلك التي في مدينه الفلوجه إلا أنها لا زالت أعلى من معدلات الدول المتقدمة والكثير من الدول النامية. وجود تغيير في حجم السائل الامنيوني بتشخيص السونار قبل الولادة قد يخفي تشوهات ولاديه خطيرة والتدخين أو التعرض للتدخين عند الحمل وصله القرابة بين الأبوين قد يعرض العائلة لإنجاب أطفال مصابين بالتشوهات الخلقية.

Objectives: To study the incidence, types, geographical distribution, and risk factors of congenital anomalies (CAs) in a teaching hospital.

Methods: A total of 5864 neonates were examined for CAs between October 2010 and October 2011 in Al-Ramadi Maternity and Children's Teaching Hospital, Al-Ramadi, Western Iraq. Data include: neonate's name, gender, weight, and type of CAs, mother's age, residence, education, parity, consanguinity, smoking, illness, drugs, and ultrasound (U/S) results, father's age and smoking, and family recurrence of CAs. For every case, 2 controls were selected. Types and incidence of CAs was calculated. Odds ratio and confidence interval was utilized for risk factors evaluation.

Results: Overall CA incidences were 40.5/1000 for total births, 40.8/1000 live births, and 270.0/1000 for stillbirths. Twenty percent of CAs was found as multiple, 80% single, 63.8% major, and 36.2% minor. The cardiovascular system was found most affected, followed by genito-urinary system. Low birth weight, male gender, maternal smoking, consanguinity, parity, and CAs family recurrence were found to be significant risk factors, and oligohydramnios, polyhydramnios, and positive CAs by U/S, found as significant co-factors associated with CAs, while parental age, and maternal education were not considered risk factors.

Conclusion: Although the incidence of CAs was lower than the Al-Fallujah rate, it is still higher than many developed and developing countries. Amniotic fluid volume changes in U/S may hide an ominous CA, and maternal smoking exposure during pregnancy and consanguinity may expose the family to a congenitally anomalous delivery.

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According to the tenth revision of the International Classification of Diseases (ICD 10), congenital anomalies (CAs) include structural malformations, deformations, chromosomal abnormalities, but not the inborn error of metabolism.[1] Every year, approximately 8 million children that comprise approximately 6% of the total worldwide births are born with serious CAs of a genetic or environmental causes, and approximately 3.3 millions of those under 5 years of age die from these anomalies, while approximately 3.2 millions of those who survive with these anomalies, continue to live, but disabled during their life.[2] These anomalies varies from a relatively minor to major structural defects. Minor CA involves non-vital organs with little or no functional effects, they do not cause any distress in the newborn, and usually there is no urgency for their correction, especially in the neonatal period. In contrast, major or severe CA may be life threatening, thus requires immediate correction.[3] The causes of CAs can be divided into genetic (multifactorial, single gene, or chromosomal abnormalities), environmental factors, and teratogenic agents, such as maternal alcoholism, diabetes, endocrinopathy, nutritional deficiency, infections, mechanical problems, chemical agents, drugs, radiation, hyperthermia, and unknown factors.[4] The impact of CA is more severe in the low and middle, than high-income countries, since 94% of those born with serious CAs in these areas die due to these anomalies.[3] The birth prevalence of CAs in developing countries is underestimated, mainly due to the deficiency of diagnostic facilities, and lack of reliability of the medical records and health statistics, so the recorded rates in these countries must be considered of a minimum estimates.[5] The aim of this study is to find out the incidence, types, and geographical distribution of structural CAs in neonates delivered in Al-Ramadi Maternity and Children's Teaching Hospital (MCTH), Western Iraq, and examined for CAs screening in the Western Iraq Center for Congenital Anomalies Registry and Surveillance (WICCARS) of the hospital, and also to identify the effect of different human variables as risk factors in the development of these morbid and mortal anomalies.

Methods. This is a cohort with nested case control, hospital base designed study to find out the incidence, types, geographical distribution and certain risk factors of structural CAs in neonates delivered in Al-Ramadi MCTH, and monitored in the WICCARS of the hospital from October 2010 to October 2011. Al-Ramadi MCTH is the main hospital (tertiary hospital) in Al-Anbar governorate for pediatrics and gynecology care, and covers most deliveries of Al-Ramadi city (the center of the governorate with 500,000 populations), and all referred pediatrics and gynecological cases from the other districts of the Governorate. The WICCARS is located in Al-Ramadi MCTH, caring by screening all neonates delivered in the hospital, looking for CAs, and planned in the future as a center for registering all anomalies recorded in the governorate. Birth certificates are not delivered to any family, unless their neonates are examined in this center. The center is directed by a trained pediatricians, and acts through full examination of all neonates delivered in the hospital from Al-Ramadi residence or those from the same residence and delivered in the hospital within the study period, but skipped the center and discovered during their readmission for any illness in the Neonatal Intensive Care Unit, Post Neonatal Admission Wards, or in the Causality Unit of the hospital, looking for CAs. Abortions of the hospital, deliveries outside the hospital, or those referred from the other districts of the governorate, and CAs for babies delivered before the study period, were excluded from the study. Stillbirths (delivery of a dead baby that died in the uterus after 20 weeks of gestational age) are examined by the delivery room doctors for any visible major structural anomalies, and a special data form for the stillbirth and the parents is filled. No autopsy or chromosomal study examination is available in the hospital. Laboratory tests, radiological, ultrasound, and ECHO examinations, or medical specialty consultations were carried out when required to help in the diagnosis of certain CAs. Any recorded CA is classified and coded according to ICD 10.[6] Collected data for the neonate includes: name, gender, birth weight, and type of CA. Data for the mother includes: age, residence, education, parity, consanguinity with her husband, exposure for passive or active smoking, drugs intake, results of her ultrasound examination (U/S), and illnesses during pregnancy (hypertension, diabetes mellitus, ante partum hemorrhage, infections, rash, and fever). Data for the father includes: age, education, and smoking history. Other data includes any recurrence of the same or different CA in the family members or their relatives. For every recorded neonate with CA, 2 consecutive non-previously registered CA-free age matched neonates were selected as controls, 2 non-anomalous healthy neonates from the center for those examined in the center, and 2 non-anomalous patients selected from the same ward of the discovered case, for those examined in the wards, and the same data form of the cases were recorded.

Statistical analysis was performed using EPI Info system version 5.3.1. Data are presented as frequency and percentages (qualitative data) with testing of

significance between different proportions was performed using Pearson Chi-Squared test at 0.05 level of significance. Odds ratio was calculated for measurement of the different variables as risk factors for developing CAs, with its 95% confidence interval was used for the assessment of the significance of the risk measurements. The Scientific Research Committee of the Medical College, Al-Anbar University, Iraq, approved the research.

Results. The total hospital deliveries during the study period was 10,122 different deliveries. The total examined neonates in the WICCARS center from Al-Ramadi residence were 5864, which is composed of 5648 neonates visited, examined, and registered in the center, and the other 216 (2.65%) neonates skipped the center, but discovered during their readmission in the hospital and registered with other neonates, and 32% of them were found associated with CAs. The rest 4358 composed of 3817 neonates from deliveries referred from other districts of the governorate and excluded from the study, and 541 (6.66%) neonates skipped the center examination but still not discovered for examination in the center. The examined 5864 neonates composed of 5742 live birth and 122 stillbirth deliveries, including 3117 males and 2747 females, with a male/female ratio of 1.13/1. The number of examined twin deliveries were 82, producing 164 twins composing 2.8% of the total examined neonates. There was no recorded twin delivery in the stillbirth deliveries.

The total recorded neonates associated with CAs were 267, among the live births were 234 and the stillbirth deliveries were 33 anomalies. Three (1.8%) of the twins were found associated with CAs. **Table 1** shows the monthly distribution and incidence of CAs in the live birth neonates. The number of recorded CAs was highest in January and March, and lowest in October and November months, and the difference between the highest and lowest numbers was statistically not significant (p=0.452), while their incidence was highest in November, January and March, and lowest in May and July months. **Table 2** shows the geographical distribution of the recorded CAs in Al-Ramadi city. The highest incidence was from Al-Mala'ab sector (75.8/1000) followed by Al-Khalideiyah (69.5/1000) sectors, and the lowest recorded incidence was from Eastern Husaibah (33/1000), and Al-Tash (35.3/1000) sectors. **Table 3** shows the gender distribution and incidence of CAs in live births, stillbirth, and total birth deliveries. The incidence of anomalies in live births was 40.8/1000 births, in stillbirths was 270/1000 births and in total births 45.5/1000 births. The number of CAs was found significantly more in males than females in both the total (p=0.001) and live birth deliveries (p=0.002), while in stillbirth deliveries, no statistical difference was recorded between males and females (p=0.751). Forty-seven (20%) of the examined anomalous cases were found as multiple CAs, and so the total number of recorded CAs was 296 anomalies, and exceeded the total recoded anomalous neonates (234). From those 296 anomalies, 189 (63.8%) were found major (incidence: 32.2/1000), and 107 (36.2%) minor anomalies (incidence: 18.2/1000). **Table 4** shows the incidence and systemic distribution of recorded CAs in

Table 1 - The monthly distribution of examined neonates, number and incidence of congenital anomalies (CAs) among live born neonates.

Months	Monthly examined neonates		Recorded CAs in males		Recorded CAs in females		Total CAs per month		Incidence/1000 patients/month
	n (%)								
October	291	(5.1)	5	(2.1)	7	(2.9)	12	(5.1)	41.2
November	249	(4.3)	9	(3.8)	5	(2.1)	14	(5.9)	56.2
December	581	(10.1)	15	(6.4)	7	(2.9)	22	(9.4)	37.8
January	502	(8.7)	20	(8.5)	7	(3.9)	27	(11.5)	53.7
February	393	(6.8)	12	(5.1)	5	(2.1)	17	(7.2)	43.2
March	480	(8.4)	13	(5.5)	12	(5.1)	25	(10.6)	52.0
April	455	(7.9)	10	(4.2)	9	(3.8)	19	(8.1)	41.7
May	740	(12.8)	16	(6.8)	6	(2.5)	22	(9.4)	29.7
June	612	(10.6)	14	(5.9)	5	(2.1)	19	(8.1)	31.0
July	553	(9.6)	9	(3.8)	11	(4.7)	20	(8.5)	36.1
August	483	(8.4)	13	(5.5)	7	(2.9)	20	(8.5)	41.4
September	403	(7.0)	11	(4.7)	6	(2.5)	17	(7.2)	42.1
Total	**5742**	**(100.0)**	**147**	**(62.8)**	**87**	**(37.2)**	**234**	**(100.0)**	**40.8**

live born neonates. Cardiovascular anomalies was found the most common recorded anomalies and comprised 29% of the total anomalies, followed by genito-urinary (16.6%), musculoskeletal (14.1%), central nervous system (CNS [11.5%]), and gastrointestinal anomalies (7.4%). Single CAs presented more in skin (89.5%), genito-urinary system (83.6%), gastrointestinal system (68.3%), and eye (66.6%) anomalies, while those presented as multiple anomalies recorded more as respiratory system (80%) and cardiovascular (53.5%) anomalies.

In cardiovascular anomalies, ventricular septal defects (VSD) were the most common recorded cardiac defects, and occupied 44% of these anomalies, followed by atrial septal defects (ASD [27%]), while in genito-urinary CAs, the undescended testis was the most common recorded anomaly (51%). Most musculoskeletal anomalies presented as single anomalies, and congenital dislocation of the hip joint (CDH) comprise 35% of these anomalies. More than 93% of CDHs presented as single CA, and their incidence was 2.6/1000 live births. The CNS anomalies found of equal distribution among single and multiple anomalies, and neural tube defects (NTDs) covered the majority (56%) of such anomalies. The incidence of NTDs was 3.3/1000 live births. In gastrointestinal anomalies, the lip and palate defects anomalies were the most common presenting CAs, and occupied approximately 36% of these anomalies. Most of the skin anomalies presents as single CAs, and the hemangioma occupied 63% of these anomalies. From the 19 recorded syndromes, 14 were found as Down syndrome (DS), and 3 as achondroplasia. The incidence of DS was 2.4/1000 live births (**Table 5**). Approximately 57% of DS were found complicated by other anomalies, and 43% as single non-complicated syndromes. The majority (75%) of complicated DS were found associated with congenital heart diseases (CHD). **Table 6** shows the distribution of risk factors between the live born anomalous cases and controls. The number of examined controls was 468 normal neonates, composed of 253 males and 215 females. The risk of developing CAs was found 4.5 times more in patients with family history of previous another CA, 4.3 times more when the pregnant mothers had polyhydramnios, 2.5 times more when she had oligohydramnius, and 31 times more when she had positive CA by U/S before delivery (when these are compared with normal U/S results), 2 times more when she had 4 or more deliveries, and 2 times more when she was a passive or active smoker (when the total of passive and active smoking mothers were compared with non-smoking mothers), and 1.5 times more if she married a relative husband. The risk was found significantly more in male gender, and in low birth weight (<2500 grams) than in normal birth or female neonates, while maternal education (when

Table 2 - The geographical distribution of recorded congenital anomalies incidences in live births of Al-Ramadi city.

Geographical sector	Examined live births		Congenital anomalies		Incidence /1000
	n	(%)	n	(%)	
Al-Mala'ab	422	(7.3)	32	(13.6)	75.8
Al-Khalidiyah	115	(2.0)	8	(3.4)	69.5
Al-Shameiyah	158	(2.7)	10	(4.2)	63.2
Al-Hoazz	116	(2.0)	7	(2.9)	60.3
Al-Sigareiah	320	(5.5)	21	(8.9)	60.0
Al-Andalus	84	(1.4)	5	(2.1)	59.5
Al-Aadil	88	(1.5)	5	(2.1)	56.8
Al-Jamiea'ah	18	(0.3)	1	(0.4)	55.5
Al-Sharikah	37	(0.6)	2	(0.8)	54.5
Al-Habbaniyah	38	(0.6)	2	(0.8)	52.6
Western Al-Jazeerah	514	(8.9)	27	(11.5)	52.5
Al-Eskan	39	(0.6)	2	(0.8)	51.2
Al-Thayyalah	202	(3.5)	9	(3.8)	44.5
Al-Sufeiyah	325	(5.6)	14	(5.9)	43.0
Eastern Al-Jazeerah	550	(9.5)	22	(9.4)	40.0
Five Kilo	329	(5.7)	13	(5.5)	39.5
Al-Ta'ameem	608	(10.5)	24	(10.2)	39.4
Al-Zangurah	204	(3.5)	8	(3.4)	39.2
Al-Warrar	132	(2.1)	5	(2.1)	37.8
Al-Thubbatt	84	(1.4)	3	(1.3)	35.7
Al-Tash	198	(3.4)	7	(2.9)	35.3
Eastern Husaibah	212	(3.6)	7	(2.9)	33.0
Other sectors	949	(16.5)	0	--	--
Total	**5742**	**(100.0)**	**234**	**100**	**40.8**

Table 3 - The incidence and gender distribution of congenital anomalies in live births, stillbirths, and total deliveries in Al-Ramadi city.

Types of birth	Overall examined neonates						Congenital anomaly associated neonates						*P*-value	Overall incidences /1000
	Number (%)		Males n (%)		Females n (%)		Number (%)		Males n (%)		Females n (%)			
Live births	5742	(98)	3043	(51.8)	2699	(46.1)	234	(87.6)	148/1000	(48.6)	86/1000	(31.8)	0.002	40.8
Still births	122	(2)	74	(1.2)	48	(0.8)	33	(12.3)	21/1000	(280)	12/1000	(250)	0.751	270.0
Total births	5864	(100)	3117	(53.1)	2747	(46.9)	267	(100)	169/1000	(54.2)	98/1000	(35.6)	0.001	45.5

Table 4 - The incidence and systemic distribution of single and multiple congenital anomalies (CAs) according to cardiovascular, genito-urinary, muscuskeletal, and central nervous system in live born neonates.

Affected system	Single CAs (n=187)		Multiple CAs (n=47)		Total		Percentage from the total CAs (N=296)	Incidence/1000 live births
Cardiovascular system								
VSD	23	(26.7)	15	(17.4)	38	(44.0)		6.6
ASD	13	(15.1)	10	(11.6)	23	(27.0)		4.0
Common AV canal	1	(1.2)	7	(8.1)	8	(9.3)		1.39
Pulmonary stenosis	--	--	6	(7.0)	6	(6.9)		1.0
PDA	2	(2.3)	4	(4.7)	6	(6.9)		1.0
TGA	1	(1.2)	1	(1.2)	2	(2.3)		0.34
Ebstein's anomaly	--	--	1	(1.2)	1	(1.2)		0.17
Hypoplastic left ventricle	--	--	1	(1.2)	1	(1.2)		0.17
Dextrocardia	--	--	1	(1.2)	1	(1.2)		0.17
Total	**40**	**46.5**	**46**	**(53.5)**	**86**	**(100)**	**29.0**	**14.9**
Genito-urinary system								
Undescended testis	21	42.8	4	(8.2)	26	(51.2)		4.52
Hypospadius	7	14.3	2	(4.1)	9	(18.1)		1.56
Hydrocele	6	12.2	--		6	(12.2)		1.04
Ambiguous genitalia	4	8.2	1	(2.0)	5	(10.2)		0.87
Vesical extrophy	2	4.1	--		2	(4.1)		0.34
Rectovesical fistula	--	--		(2.0)	1	(2.1)		0.17
Bartholin gland cyst	1	2.0	--	--	1	(2.1)		0.17
Total	**41**	**(83.6)**	**8**	**(16.3)**	**49**	**(100)**	**16.6**	**8.5**
Musculoskeletal system								
CDH	14	(33.3)	1	(2.4)	15	(35.7)		2.61
Club foot	6	(14.2)	2	(4.8)	8	(18.9)		1.39
Polydactyly	5	(11.9)	1	(2.4)	6	(14.2)		1.0
Absent fingers	3	(7.1)	--	--	3	(7.1)		0.52
Syndactyly	1	(2.4)	1	(2.4)	2	(4.8)		0.34
Micrognathia	1	(2.4)	1	(2.4)	2	(4.8)		0.34
Claw hand	-		1	(2.4)	1	(2.4)		0.17
Sacrococcegeal teratoma	1	(2.4)	--		1	(2.4)		0.17
Arthrogrypsis	-		1	(2.4)	1	(2.4)		0.17
Short one upper limb	-		1	(2.4)	1	(2.4)		0.17
Absent one leg	-		1	(2.4)	1	(2.4)		0.17
Amelia	1	(2.4)	-		1	(2.4)		0.17
Meromelia	1	(2.4)	-		1	(2.4)		0.17
Total	**32**	**(76.1)**	**10**	**(23.8)**	**42**	**(100)**	**14.1**	**7.3**
Central nervous system								
Hydrocephalus	3	(8.8)	6	(17.6)	9	(26.4)		1.56
Meningomyelocele	5	(14.7)	2	(5.9)	7	(20.5)		1.21
Encephalocele	3	(8.8)	2	(5.9)	5	(14.7)		0.87
Microcephaly	-		4	(11.7)	4	(11.7)		0.69
Spina bifida occulta	3	(8.8)	--	--	3	(8.8)		0.52
Anencephaly	2	(5.9)	--	--	2	(5.9)		0.34
Spina befida aperta	--		2	(5.9)	2	(5.9)		0.34
Flat occepit	--		1	(2.9)	1	(2.9)		0.17
Craniosynostosis	1	(2.9)	--		1	(2.9)		0.17
Total	**17**	**(50.0)**	**17**	**(50.0)**	**34**	**(100)**	**11.5**	**5.9**

VSD - ventricular septal defect, ASD - atrial septal defect, PDA - patent ductus arteriosus, TGA - transposition of great arteries, CDH - congenital dislocation of hip joint

Table 5 - The incidence and systemic distribution of single and multiple congenital anomalies (CAs) according to gastrointestinal, skin, syndromes, ear, eye, respiratory, and endocrine system in live born neonates.

Affected systems	Single CAs (n=187) n (%)	Multiple CAs (n=47) n (%)	Total CAs n (%)	Percentage from the total CAs (N=296)	Incidence/1000 live births
Gastrointestinal system					
Lip and palate defects	4 (18.1)	4 18.1	8 (36.3)		1.39
Cleft lip and palate (n=4)	4 (1.0)	1 (3.0)			
Cleft lip (n=3)	3 (2.0)	3 (1.0)			
Cleft palate (n=1)	1 (1.0)	--			
Imperforate anus	2 (9.1)	2 (9.1)	4 (18.1)		0.69
Tongue tie	2 (9.1)	-- --	2 (9.1)		0.34
Anal stenosis	1 (4.5)	-- --	1 (4.5)		0.17
Duodenal atresia	1 (4.5)	-- --	1 (4.5)		0.17
Diaphragmatic hernia	1 (4.5)	-- --	1 (4.5)		0.17
Omphalocele	1 (4.5)	-- --	1 (4.5)		0.17
Esophageal atresi	-- --	1 (4.5)	1 (4.5)		0.17
Umbilical hernia	1 (4.5)	-- --	1 (4.5)		0.17
Inguinal hernia	1 (4.5)	-- --	1 (4.5)		0.17
Ranula	1 (4.5)	-- --	1 (4.5)		0.17
Total	**15 (68.3)**	**7 (31.7)**	**22 (100.0)**	**7.4**	**3.8**
Skin					
Hemangioma	10 (52.6)	2 (10.5)	12 (63.1)		2.08
Skin tag	4 (21.0)	-- --	4 (21.0)		0.69
Ecthyosis	1 (5.3)	-- --	1 (5.3)		0.17
Epidermolysis bullosa	1 (5.3)	-- --	1 (5.3)		0.17
Cystic hygroma	1 (5.3)	-- --	1 (5.3)		0.17
Total	**17 (89.5)**	**2 (10.5)**	**19 (100.0)**	**6.4**	**3.3**
Syndromes					
Down syndrome	6 (31.5)	8 (42.0)	14 (73.6)		2.43
Achondroplasia	3 (15.7)	-- --	3 (15.7)		0.52
Turner syndrome	1 (5.3)	-- --	1 (5.3)		0.17
Pierre robin syndrome	1 (5.3)	-- --	1 (5.3)		0.17
Total	**11 (58.0)**	**8 (42.0)**	**19 (100.0)**	**6.4**	**3.3**
Ear					
Accessory auricle	5 (55.5)	1 (11.1)	6 (66.6)		1.04
Low set ears	-- --	3 (33.3)	3 (33.4)		0.52
Total	**5 (55.5)**	**4 (44.6)**	**9 (100.0)**	**(3.0)**	**1.56**
Eye					
Aniridia	2 (22.2)	1 (11.1)	3 (33.3)		0.52
Hypertelorism	-- --	2 (22.2)	2 (22.2)		0.34
Microphthalmia	2 (22.2)	-- --	2 (22.2)		0.34
Cataract	2 (22.2)	-- --	2 (22.2)		0.34
Total	**6 (66.6)**	**3 (33.3)**	**9 (100.0)**	**(3.0)**	**1.56**
Respiratory system					
Laryngomalacia	-- --	2 (40.0)	2 (40.0)		0.34
Coanal atresia	1 (20.0)	-- --	1 (20.0)		0.17
Nasal polyp	-- --	1 (20.0)	1 (20.0)		0.17
Bilateral absent alai nasai	-- --	1 (20.0)	1 (20.0)		0.17
Total	**1 (20.0)**	**4 (80.0)**	**5 (100.0)**	**(1.7)**	**0.8**
Endocrine system					
Hypothyroidism	1 (100.0)	-- --	1 (100.0)		0.17
Total	**1 (100.0)**	-- --	**1 (100.0)**	**(0.3)**	**0.17**
Over all total	**187 (63.2)**	**109 (36.8)**	**296 (100.0)**	**(100.0)**	**51.5**

Table 6 - The distribution of certain risk factors between cases and controls in live born neonates.

Risk factors	Cases	Controls	Odd ratio	(95% confidence interval)	*P*-value
Baby					
Gender					
Male	151	253	1.55	(1.10-2.17)*	0.008
Female	83	215			
Birth weight					
<2500	42	55	1.64	(1.04-2.60)*	0.025
≥2500	192	413			
Mother					
Residence					
Rural	128	244	1.11	(0.80-1.54)	0.5213
Urban	106	224			
Age, years					
≤20	39	87	0.89	(0.58-1.38)	0.5991
21-30	130	287			
31-40	54	80			
>40	11	14	1.57	(0.65-3.75)	0.2734
Parity					
<4	102	291			
≥4	132	177	2.13	(1.53-2.96)*	0.0001
Education					
Illiterate	62	154	0.76	(0.52-1.10)	0.1241
Primary	116	228			
Secondary	35	56			
High education	21	30	1.32	(0.70-2.47)	0.3615
Consanguinity					
Related	159	279	1.44	(1.02-2.03)*	0.031
Not related	75	189			
Smoking					
Passive	136	186	2.08	(1.50-2.91)*	0.0001
Active	1	3		-	
Non-smoker	97	279			
Illnesses					
Infections	101	187	1.16	(0.82-1.63)	0.3760
Hypertension	15	31	1.04	(0.51-2.09)	0.9097
Diabetes	2	1		-	
Normal	116	249			
Ultrasound result					
Normal	188	441			
Oligohydramnios	18	17	2.48	(1.19-5.18)*	0.007
Polyhydramnios	11	6	4.3	(1.45-13.26)*	0.002
Fetal anomaly	14	1	31.4	(4.29-643.2)*	0.000
Others	3	3		-	
Drugs					
Folic acid + iron	5	8	0.96	(0.28-3.92)	0.9507
Folic acid + iron + others	181	386	0.72	(0.47-1.1)	0.1146
Drugs not used	48	74			
Father					
Age					
≤20 yrs	6	13	0.95	(0.32-2.74)	0.9231
21-30	127	259			
31-40	75	158			
>40	26	38	1.47	(0.84-2.56)	0.125
Smoking					
Smoker	83	148	1.19	(0.84-1.68)	0.306
Non-smoker	151	320			
Family history of CAs					
Positive	15	7	4.51	(1.70-12.39)*	0.0004
Negative	219	461			

*Significant, CAs - congenital anomalies

each of the illiterate and high educated mothers were compared with the total of primary and secondary educated mothers), paternal smoking and parental age (when the ≥40 or the ≤ 20 parents were compared with the 21-39 years age group parents), and type of residence (rural or urban) were found not a significant risk factors for development of these anomalies. For the risk of the drug intake during pregnancy, the study showed 48 (20.5%) of mothers producing CAs took no drugs during their pregnancy period, 5 (2.1%) took folic acid and iron (Ferro folic tablet) only, and 181 (77.3%) took different types of drugs including different antibiotics, antihypertensive, analgesics, antimicrobials for congenital infections, and hormones, with the folic acid and iron therapy, and no significant relation was found between these drug intake and the occurrence of CAs, and no recorded mother found taking the folic acid alone, neither during her pregnancy nor during her pre-conceptual period.

Discussion. Most children born with major CAs and survive their infancy are affected physically, mentally or socially, and can be of increased risk for morbidities and mortalities due to various health disorders.[7] In the present study, the overall incidence of CAs was 45.5/1000 (4.5%). This was lower than what was recorded in Al-Fallujah district, where they recorded an incidence of 15% in 2010,[8] but higher than the Al-Basrah incidence in southern Iraq in 2000 (17.6/1000 live births),[9] also was higher than what was recorded in Iran (1.01%),[10] Arab Emirates (0.79%),[11] Kuwait (1.2%),[12] Oman (2.46%),[13] United States (3%),[14] and Turkey (2.9%)[15] countries. Inspite of Al-Fallujah being only 45 km to the east of Al-Ramadi city, the very high incidence of CAs in this city may be because the city involved in a unique war in the recent decades, when it was rained by different shells, bombs, and rockets before it was infiltrated by the US army in 2004, when after termination of the battle, most of the houses were found burned, or destroyed by this infiltration. The explosions and burning materials were found containing different contaminants and metals as depleted Uranium (DU) and other contaminants.[8] Such infiltration and house burning did not occurred in Al-Ramadi city, but it showed a long intermittent explosions and military actions that damaged the basal infrastructure and contaminated the environment, and could be one of the causes of this high incidence of CAs when compared to some developing and developed countries, in addition to the different racial, ethnic, social, geographical, nutritional, and socioeconomic factors, and type of samples and criteria of diagnosis of these countries.

The highest incidence of CAs was recorded in November, January, and March, and the lowest in May and June months. Apart from the variation in the number of examined neonates for every month, no clear explanation is available to explain the monthly variations of the incidence of these CAs. Regarding the geographical distribution of these CAs in Al-Ramadi city, the highest CAs incidence was recorded in Al-Malaa'b and Al-Khalideiyah sectors, and the lowest in the Eastern Husaibah and Al-Tash sectors. These variations could be due to the difference in the population density, level of sanitary services, environmental contamination, number and types of explosions, and the number and types of the previous military activities. The present study reported that the most recorded CAs were cardiovascular anomalies (29%). The same result was recorded in India[16] and Malta[17] studies, while in Turkey the CNS system,[15] in Iran the musculoskeletal system,[10] and in Saudi Arabia the alimentary system anomalies.[18] The high cardiovascular record in this study may be due to the applied full examination of every neonate after his seventh birthday to detect congenital heart or other anomalies, which may have no signs for diagnosis at birth. The overall cardiovascular anomalies incidence was 14.6/1000, and the VSD and ASD cardiac defects was found the most common recorded anomalies. This incidence was higher than Al-Ani[19] overall cardiovascular anomalies incidence in the same hospital (10/1000), but consistent with the same Al-Ani study result when VSD and ASD defects found also the most common recorded cardiac anomalies.

The second recorded anomalies was genito-urinary systems (16.8 %), followed by musculoskeletal system (14%), CNS (11.5 %) and gastrointestinal system (7.4%) anomalies. This was different than what recorded in Hungary[2] when they reported genito-urinary system the most common anomalies (31.1%), followed by cardiovascular (27%), alimentary (9.6%), CNS (7.5%) and skeletal system (7.2%) anomalies, and from what was recorded in India,[20] when they reported both gastrointestinal and genito-urinary the highest recorded anomalies (26%), followed by musculoskeletal (23%), cardiovascular (11%), and CNS (6%) anomalies. Regarding CNS anomalies, the incidence of NTDs was 3.3/1000. This was typical to what was recorded by Al-Ani et al record in 2010[21] in the same research hospital when they recorded NTDs incidence also 3.3/1000 live births.

In musculoskeletal anomalies, CDH incidence was found to be 2.6/1000. This was higher than the Brazil (0.53/1000)[22] and Iran (1.87/1000) studies.[23] Down syndrome incidence was found 2.4/1000. This was higher than that of Iran (0.6/1000),[9] Brazil (0.63/1000),[22] and Canada (1.44/1000) studies.[24] Males were found significantly more affected and a risk factor increasing the CAs than females, which was consistent with other studies.[10,16,25-27] Male dominance of CAs may be due to the increased male associated genito-urinary system anomalies, X-linked male associated diseases and anomalies, and the oxidative stress associated anomalies as cyanotic CHDs.[27]

From the stillbirth deliveries, 33 (27%) were found associated with CAs, which was higher than the results from Iran (12.5%),[23] and Kuwait (11%)studies.[12]

In the present study, single anomaly was found 4 times (80%) more than multiple anomalies (20%). This was consistent to the result of Brazil study,[22] while in Kuwait,[10] multiple CAs was found more than single CAs. Our study recorded major (63.8%) more than minor CAs (36.2%), which was consistent with the Kuwait result,[12] while in India,[28] minor was found 4 times more than the major anomalies. Low birth weight was found significantly increasing CAs. This was consistent with studies in Egypt,[29] and the United States.[30]

Oligo and polyhydramnios by U/S examination were found a significant co-factors that herald a CA. The same relation was noticed with other studies,[28,31,32] also the prenatal diagnosis of CAs was found consistent with the findings of other studies.[30,33] Maternal aging may increase her exposure to hypertension, diabetes, obesity, and to chromosomal abnormality affected fetuses associated with CAs. In the present study, no relation was found between maternal age and CAs. This was consistent to Al-Ani's study in the same hospital in 2010,[19] when he reported no relation of CHDs with advancing maternal age, while other studies showed maternal age is an important risk factor for developing CAs.[29,34] This diverse result may be due to the social trend of this tribal populated area to start female marriage early, and so increasing her parity in her twentieth age, and become more liable to produce anomalous neonates in her early twentieth ages, since more than 72% of those neonates were found from mothers less than 30 years of age. Congenital anomalies was found significantly more in consanguineous than non-consanguineous families. The same relation was noticed in other studies,[35-37] and also by Al-Ani study[19] in the same hospital, when he reported parental consanguinity a significant risk factor exposing for CHDs.

Passively smoking pregnant mothers who breathe from a second-hand smoke are at increased risk for delivering stillbirths, or babies affected with skull defects, missing or deformed limbs, clubfoot, cleft palate, and congenital heart anomalies.[38] Dr. Jo Leonardi-Bee of the UK Centre for Tobacco Control Studies at the University of Nottingham said: "Since passive smoking involves exposure to the same range of tobacco toxins experienced by active smokers, albeit at lower levels, it is likely that, coming into contact with second-hand smoke also increases the risk of some of all of these complications". He added also that: "The risks are related to the amount of cigarettes that are smoked--the data suggests that being exposed to around 10 cigarettes a day is enough for the risks to be increased, so it is therefore very important for men to cut down".[39] Recent studies reported that cigarette smoking reduces the fetal serum level of folic acid.[40] Other studies centers on the carbon monoxide effect, which was found to reduce the oxygen carrying capacity to the fetal tissue, and the nicotine which crosses the placenta, and reduces the uterine blood flow, affecting fetal oxygenation and the acid-base balance, leading to CAs.[41] In the present study, smoking was found a significant factor increasing CAs. The same result was confirmed by other studies.[29,42] The number of passive smoking mothers in our study was found exceeding their smoking husbands because maternal exposure may be from her husband, other family members, or from a smoking relative living within their home, together.

Studies showed the recurrence risk of malformation in siblings as well as offspring of affected individuals is relatively high when compared with the population frequency, which points toward the genetic factors in causing these anomalies.[43] In our study, both the family recurrence of CAs and the parental consanguinity found significantly increasing the development CAs, which also points toward the genetic factor causing these anomalies. The same risk of CAs recurrence with parental consanguinity were also noticed in Egypt study,[29] and also in this hospital by Al-Ani study[19] when he reported 33.3% of ASDs, 19% of VSDs, and 10% of Tetralogy of Fallots associated with another family history of CHDs.

No relation between the drug intake and occurrence of CAs was noticed in this study, and no significant decrease of CAs incidence was noticed in mothers taking folic acid, which could be because all taken folate was during pregnancy with iron, and none of the folate was taken during the pre-conceptual period. Absence

of pre-conceptual folic acid intake of pregnant mothers was also noticed in the same hospital by Al-Ani study in 2010.[21]

Diseases of respiratory system caused by acute infections are among the most common maternal diseases during pregnancy, and infections known to produce CAs were well known associated with the congenital infection acronym "TORCH" (Toxoplasmosis, Others, Rubella, Cytomegalovirus, Herpes).[44,45] Although the study did not involve the types of infections of the pregnant mothers, the number of recorded CAs were found higher in pregnant infected than non-infected mothers.

The incidence of CAs may be underestimated because some of the neonates delivered in the hospital skipped the center examination and not enrolled in the study, and either they received their surgical or medical treatment in a private or different hospital, or may not discovered during their readmission in the hospital, or may have died outside the hospital. The absence of autopsy and chromosomal study in the hospital makes some of the stillbirth and chromosomal abnormality associated CAs not discovered, and so, not registered with these CAs.

In conclusion, the incidence of CAs in Al-Ramadi MCTH hospital was found to be high. When compared with other studies, the incidence was found lower than that of Al-Fallujah hospital, but still was higher than Al-Basrah incidence in the south of Iraq, and of many developed and developing countries. Amniotic fluid volume changes on U/S examination may hide an ominous CA, and smoking exposure during pregnancy and parental consanguinity may expose the mother to produce a congenitally anomalous deliveries. Social education utilizing multimedia systems, such as TV, magazines, and health center programs regarding the risk of passive and active smoking, and consanguinity marriages is important to reduce the incidence of these CAs.

A more in-depth analytic research is needed to determine the possible genetic, socio-demographic, and environmental factors, such as war explosions and heavy metals contaminants like depleted Uranium that may underlay the high incidence of these CAs.

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