Profile of Chromosomal Abnormalities in the Al Jahra Region of Kuwait

R.L. Al-Naggar^a S.A. Mady^b S.M. Tayel^a T.I. Farag^a
S.A. Al-Awadi^a M.M. Al-Ghanim^b S.J. Abulhasan^a M.A. Sabry^a
L. Bastaki^a

^aMedical Genetics Centre, Maternity Hospital, and

^bPaediatric Department, Al-Jahra Hospital, Kuwait

Key Words

Chromosomal abnormalities, numerical and structural · Down's syndrome · Trisomy 18 · Deletion · Duplication · Inversion

Abstract

Objective: One hundred and seventy-seven newborn babies with chromosomal abnormalities were studied at the Al-Jahra satellite clinic of the Kuwait Medical Genetics Centre (KMGC), Kuwait, over a 7-year period from January 1983 to December 1989 to make a reanalysis and recomputation of the statistical results of the previous short-term studies.

Methods: The data were collected from the registry of chromosomal abnormalities and from the clinical records of the patients in KMGC retrospectively. Controls were selected from the newborn babies delivered in the same period of study. The logistic regression analysis was computed using dependent/independent variables. **Results:** Ninety-five percent of the cases had numerical chromo-

somal abnormalities, and 5% had structural chromosomal abnormalities. One hundred and forty-five cases had classic trisomy 21, with an incidence of 2.9/1,000 live births (LB), 16 cases had trisomy 18 (0.3/1,000 LB), 5 cases had trisomy 13 (0.1/1,000 LB), 1 case had triploidy 69, XXY (0.02/1,000 LB) and 1 had Turner's syndrome (0.05/1,000 female LB). Nine cases with structural chromosomal abnormalities were enumerated, dir dup(1)(p21–p32), del(1)(q32–q42), del(13)(q22–q34) and inversion Y chromosome, the incidence was 0.02/1,000 LB for each. Two cases of translocation trisomy 21 (0.04/1,000 LB) and 3 cases of cri-du-chat (0.06/1,000 LB) were enumerated too. Bedouins had a double-fold increased risk of trisomy 21 (odds ratio = 1.819, $p = 0.032$), and advanced maternal age was also a risk factor while paternal age showed inconsistent pattern of risk. **Conclusion:** This study confirmed the high incidence of the common trisomies and the role of advanced maternal age and the Bedouin ethnicity as a risk factor.

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Dr. R.L. Al-Naggar
Kuwait Medical Genetics Centre
PO Box 31121
80901 Sulaibikhat (Kuwait)

Introduction

Chromosomal abnormalities involve numerical and structural aberrations. The loss or duplication of an individual and/or the entire set of chromosomes is referred to as aneuploidy. Structural rearrangement results from chromosomal breakage followed by abnormal reunion. The common structural aberrations include translocation (balanced, unbalanced, reciprocal and robertsonian), deletion, inversion, duplication, ring chromosome and isochromosome [1]. Chromosomal analysis was ascertained at the Al-Jahra Hospital, Kuwait, which serves an Arab population of about 300,000, 80% of whom belong to the Bedouin ancestry. Most of the studies on chromosomal abnormalities carried out in the same area were not comprehensive [2–8]. Classic trisomy 21 and trisomy 18 were the most common trisomies. There was also clustering of cri-du-chat syndrome [46, XY, del(5)(p14)]. The aim of this relatively long-term study was to provide a more comprehensive profile of the chromosomal abnormalities in the Al-Jahra region of Kuwait, and to compare the findings with the world-wide surveys.

Patients and Methods

The study population included 177 cases of chromosomal abnormalities from among 49,174 live births registered at the Al-Jahra Hospital from January 1983 to December 1989. Data in this retrospective study were collected from the registry for chromosomal abnormalities of the Kuwait Medical Genetics Centre and from the patients' clinical records. The data included history of the patient, a three-generation deep family pedigree, thorough clinical evaluation, cytogenetic results and statistical analysis of the risk factors such as ethnicity, maternal and paternal age effect. A group-matched case control study was undertaken in which 145 healthy live births were used as controls for the 145 trisomy-21 cases. Controls were selected from the newborns delivered during the same month of the

Table 1. Frequency/incidence of numerical and structural chromosomal abnormalities

Chromosomal abnormality	Cases n	Frequency %	Incidence per 1,000 live births
Numerical	168	94.9	3.4
Structural	9	5.1	0.2
Total	177	100.0	3.6

Table 2. Classification/percentages of Down's syndrome cases

Trisomy 21	Cases	
	n	%
Regular type	144	97.9
Mosaic	1	0.7
Translocation	2	1.4 ^a
Total	147	100

^a This low frequency of translocation 21 cases could be explained by the possibility of missing cases before the clinical and the cytogenetic assessments.

birth of the trisomy 21 cases. Logistic regression analysis was carried out using the variable status (0 for controls, and 1 for trisomy 21 cases) as the dependent variable, and ethnicity, maternal and paternal age as independent variables.

Results

Cases with chromosomal abnormalities represented 16.7% of the total number of cases with congenital malformations (948 cases) ascertained in the present study. The frequency and the incidence of numerical versus structural chromosomal aberrations are shown in table 1. Down's syndrome cases represented 83.1% of the total chromosomal abnormalities. Classical Down's syndrome presented

Table 3. Crude incidence and sex ratio among numerical chromosomal aberration cases

Numerical chromosomal aberration	Cases n	Sex ratio M/F	Incidence per 1,000 liver births
Regular Down's syndrome	145	2:1	2.9
Trisomy 18	16	1:3	0.3
Trisomy 13	5	1:4	0.1

Table 4. The risk of trisomy 21 by maternal age at delivery

Maternal age, years	Risk	Rate per 1,000	Relative risk
20	1/1,917	0.52	1.00
21	1/1,739	0.58	1.10
22	1/1,190	0.84	1.61
23	1/874	1.14	2.19
24	1/663	1.51	2.89
25	1/598	1.67	3.20
26	1/536	1.86	3.57
27	1/480	2.08	3.99
28	1/316	3.16	6.06
29	1/276	3.62	6.93
30	1/209	4.78	9.16
31	1/181	5.52	10.57
32	1/153	6.54	12.51
33	1/128	7.81	14.95
34	1/120	8.33	15.95
35	1/112	8.93	17.09
36	1/107	9.34	17.89
37	1/104	9.62	18.40
38	1/83	12.50	23.06
39	1/63	15.87	30.38
40	1/61	16.39	31.38
41	1/60	16.66	31.90
42	1/43	23.26	44.51
43	1/32	31.25	59.81
44	1/23	43.50	83.22

χ^2 for linear trend = 189.9; $p < 0.001$.

Table 5. The risk of trisomy 21 by paternal age at delivery

Paternal age, years	Risk	Rate per 1,000	Relative risk
20	1/2,798	0.36	1.00
21	1/2,600	0.38	1.08
22	1/1,593	0.63	1.76
23	1/1,466	0.68	1.91
24	1/790	1.27	3.54
25	1/599	1.67	4.67
26	1/535	1.87	5.23
27	1/411	2.43	6.81
28	1/254	3.93	11.02
29	1/225	4.44	12.44
30	1/201	4.98	13.92
31	1/192	5.21	14.57
32	1/180	5.56	15.54
33	1/171	5.85	16.36
34	1/162	6.17	17.27
35	1/161	6.21	17.27
36	1/153	6.54	18.29
37	1/140	7.14	19.99
38	1/132	7.58	21.20
39	1/121	8.26	23.12
40	1/101	9.90	27.70
41	1/95	10.52	29.45
42	1/82	12.20	34.12
43	1/73	13.70	38.33
44	1/65	15.38	43.05

χ^2 for linear trend = 122.1; $p < 0.001$

97.9%, mosaic type 0.7% and translocation type 1.4% of the total trisomy 21 cases (table 2). Table 3 shows the incidence and sex ratio of the common trisomies. Tables 4 and 5 show the risk of trisomy 21 by maternal and

paternal age at delivery. Both tables show the χ^2 and the p value. It was found that there is an increase in trisomy 21 as either maternal or paternal age increases. Table 6 shows the adjusted odds ratio for the risk factors and their

Table 6. Logistic regression analysis of 145 trisomy-21 cases and 145 controls

Variable	Odds ratio	95% confidence interval	p value
Non-Bedouin	Ref.	–	–
Bedouin	1.819	1.052–3.145	0.032
Maternal age			
↑20	Ref.	–	–
30–	3.039	1.829–5.049	<0.001
40+	5.695	1.964–16.519	0.001
Paternal age			
↑20–	Ref.	–	–
30–	4.832	2.849–8.193	<0.001
40+	2.148	0.855–5.396	0.104

95% confidence intervals after fixing the confounding effects. Bedouins are subjected to almost twofold risk of trisomy 21 as against the non-Bedouins (odds ratio = 1.819, $p = 0.032$). As the maternal age increases (30–39 years) the risk of trisomy 21 is nearly tripled as compared to a lower age group (20–29 years). The maternal age group of 40+ carries more than 5 times the risk for trisomy 21 in comparison to the age group of 20–29 years. On the other hand, paternal age showed a non-linear pattern. As the paternal age increases to the age group of 30–39 years, the risk increases 4 times in comparison to the age group of 20–29 years. In the paternal age of 40+ years, the risk was twofold higher than that of the young paternal age group.

Discussion

Several previous reports and communications regarding chromosomal aberrations observed at the Kuwait Medical Genetics Centre have been published [2–4, 6, 7, 9–11]. The overall incidence of numerical chromosomal

abnormalities in the present study was 3.4/1,000 live births which is similar to the incidence reported in Evan's [12] study. At the same time the incidence of trisomy 21 was 2.9/1,000 live births, which is close to the figure reported by Farag et al. [2] in the same region. Both figures are higher than the 1.1/1,000 live births previously reported from Kuwait [10], but similar to the incidence reported for Down's syndrome among Negev Bedouins [13], and close to that reported in west Jerusalem [14]. The difference between the figures reported in the Al-Jahra region and that reported in other regions of Kuwait could be explained by the population pattern in this area (80% Bedouins) and the high rate of consanguineous marriage among those people. The average inbreeding coefficient (ΣF) of babies with different autosomal trisomies was 0.044, which is higher than that computed from other regions of Kuwait ($\Sigma F = 0.0219$) [2–5]. In the present study, 2 cases of translocation type of trisomy 21 were reported with an incidence of 0.04/1,000 live births which is close to the incidence reported by Wright et al. [15]. Hamerton [16] and Giraud and Mattei [17] reported double and triple the figure reported by us, respectively. The difference between the figures in the present study and those of the other studies could be explained by the possibility of missing some cases before the clinical and the cytogenetic assessments. In the present study, the sex ratio for trisomy 21 was M:F 2.1:1, which is similar to that reported by DeGrouchy and Turleau [1] and double that reported by Bernheim et al. [18] (M:F 1:1). The incidence of trisomy 18 (0.3/1,000 live births) in our study is higher than the incidence (0.1/1,000 live births) reported by Sumnit [19] and Nelson et al. [20]. Even though our figure is lower than that reported earlier from the Al-Jahra Regional Hospital (0.6/1,000 live births) [2], it seems to be more realistic, as the earlier figure was calculated

for 1 year only. However, both figures confirmed trisomy 18 clustering in Kuwait. In the present study, trisomy 18 sex ratio showed preponderance to females (1M:3F), which is similar to the ratio reported by Schinzel [21]. The incidence of trisomy 13 was 0.1/1,000 live births in our study and is similar to some of the earlier reports [22, 23]. Trisomy 13 sex ratio also shows a female preponderance (M:F 1:4), which is similar to the reports of Magenis et al. [23]. The present study includes a case of Turner's syndrome, with an incidence of 0.05/1,000 female live births. This incidence is considered low when compared to earlier reports that show double [24] and even 6 times [25] our figure. The difference between our figure and the other figures could be explained by the possibility of underestimation of the diagnosis of Turner's syndrome among newborns. Our study included 3 cases of cri-du-chat with an incidence of 0.06/1,000 live births, which is higher than the incidence reported by Niebuhr [26]. Other studies carried out in Kuwait reported a similar figure [3, 11]. Our computed figure is considered triple the Danish figure reported by Niebuhr [27]. Our study confirms the clustering of cri-du-chat in Kuwait among Bedouins, which is so similar to the study by Farag et al. [3]. The other numerical and structural chromosomal abnormality cases are scarce and unreliable for statistical analysis. A question raised is, does the high consanguinity rate among Bedouins contribute to structural as well as numerical chromosomal abnormalities? We computed the risk of trisomy 21 among the liveborn babies included in our study in relation to the ethnicity, maternal and paternal age. Statistical analysis for the linear trend (chi-square) showed a significant increase in trisomy 21 as the maternal age increases ($p = 0.001$), which is highly significant while the paternal age effect was inconsistent. Hook [28] studied the maternal age effect on the

incidence of trisomy 21 and reported an increased risk with the increase in maternal age above 35 years. At the same time he suggested that the increased risk at age <15 years may result from reporting errors and not from biological differences. The adjusted odds ratio for the risk factor confirmed the effect of ethnicity (Bedouins) as a risk factor for increasing trisomy 21 ($p = 0.032$), which is a significant value. Advanced maternal age as a risk factor is also confirmed by the logistic regression ratio ($p = 0.001$) which is highly significant. Little et al. [29] studied the effect of ethnicity and maternal age effects on the risk of chromosomal abnormality among the live-born offspring. They reported an increase in the risk for trisomy-21 syndrome with advanced maternal age >35 years using the same statistical parameters [29]. On the other hand Yoon et al. [30] found that the association with meiosis 11 implies that there is at least one maternal age-related mechanism acting around the time of conception.

Conclusion

The present study confirmed the effect of ethnicity (Bedouins) and the advanced maternal and paternal age on the risk of having trisomy-21 babies. The paternal age had an inconsistent pattern. This study also confirmed the clustering of trisomy-18 and cri-du-chat syndromes in Kuwait.

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