Medical Journal of Babylon
Vol. 14- No. 2 : 389 - 401, 2017
http://www.medicaljb.com
ISSN 2312-6760©2017 University of Babylon

Original Research Article

Clinical and Cytogenetic Profile in Patients with Down Syndrome in Duhok Province, Iraq

Dian Jamel Salih[1*] Nizar Bakir[2] Adil Abo Azeez Eissa[1] Nasir A. Al-Allawi[1]
[1]College of Medicine, University of Duhok, Duhok, IRAQ
[2]Hivi Pediatric Hospital, Duhok City, Duhok, IRAQ

[*]E-mail:dian.jamel@uod.ac

Accepted 18 June, 2017

Abstract

Down syndrome is the most common Aneuploidy in humans which is associated with developmental delay, mental retardation and several characteristic physical features. This study is aimed to determine the proportion and types of chromosomal abnormalities in patients with Down syndrome in Duhok province, Iraq, and to study the clinical profile of these patients. A retrospective analysis was performed on the case records of 86 patients confirmed clinically as Down syndrome from October 2014 to April 2015, for all enrolled cases cytogenetic analysis had done at Research Centre at College of Medicine\ University of Duhok. Among the 86 cases of Down syndrome presented over a period of 6 months, non-disjunction was present in 79 (91.9%) cases, translocation in 5 (5.8%) cases and Mosaicism in 2 (2.3%) cases. The age of the enrolled patients were ranged from 1 day to 35 years, from these patients, 37 (43%) were males and 49 (57%) were females with male to female ratio of 1:1.3. The maternal ages at the time of delivery of index babies were ranged from 21 years to 47 years. The most prominent characteristic features noted were epicanthic folds (80.2%), upslanting palpebral fissures (70.9%), protruding tongue (67.4%), sandal gap (64%), depressed nasal bridge (62.8%), and flat facial features (58.1%). Congenital heart disease seen in (26.7%) and hypothyroidism seen in (10.5%)
Down syndrome mostly result from non-disjunction and efforts to establish early diagnosis and a proper screening for high association with systemic anomalies should be undertaken among the Down syndrome patients in our population.

Key Words: Down syndrome, karyotypes, mosaic, nondisjunction,

الملف السريري والوراثي الخلوي لدى الأشخاص الذين يعانون من متلازمة داون في محافظة دهوك، العراق

الخلاصة

متلازمة داون هي عبارة عن عدم توازن الكروموسومات الأكثر شيوعا في البشر مع حدوث ١ لكل ٦٥٠- ١٠٠٠ حالة ولادة. أنه يرتبط مع التأخر في النمو والتخلف العقلي والعديد من الميزات الجسدية. بالإضافة إلى ذلك، الاشخاص الذين يعانون من متلازمة داون تزيد عندهم مخاطر الإصابة بأمراض القلب الخلقية، سرطان الدم و مرض الزهايمر. يهدف هذه الدراسة الى دراسة الملف الشخصي السريري للمرضى الذين يعانون من متلازمة داون و تحديد نسبة وأنواع الشذوذ الكروموسومي. اجريت هذه دراسة رجعية لملفات المرضى، تحليل على ٨٦ من المرضى الذين يعانون من متلازمة داون من خلال تحليل وراثي خلوي في مركز البحوث بكلية العلوم الطبية\ جامعة دهوك .من بين ٨٦ حالة متلازمة داون على مدى ٦ أشهر، وجد ان عدم الانفصال في ٧٩ (٩١,٩٪) من الحالات، الإزفاء في ٥ (٥,٨٪) من الحالات و الفسيفساء في ٢ (١,٣٪) من الحالات. وكان متوسط العمر لهؤلاء المرضى ٨,٣ سنوات. وكان متوسط عمر الأم عند ولادة الطفل المصاب ٣٢,٣ عاما. و كانت أبرز السمات المميزة، طيات فوق المآقي (٨٠,٢٪)، شقوق الجفن (٧٠,٩٪)، تبارز اللسان (٦٧,٤٪)، فجوة الصندل (٦٤٪)، تسطح جسر الأنف (٦٢,٨٪)، البروفايل

الوجهي المسطح (٥٨,١ ٪).تم تشخيص تأخر في النمو في (٣٨,٤٪)من الحالات، ونقص التوتر في (٣٢,٦٪) من الحالات، وأمراض القلب الخلقية في (٢٦,٧٪) من الحالات و القصور الدرقي في (١٩,٨٪) من الحالات. في أغلب الأحيان تنتج متلازمة داون من حالة عدم انفصال الكروموسوم رقم ٢١، و ينبغي بذل الجهود لإنشاء التشخيص المبكر و اجراء فحصوصات الوراثية للأشخاص الذين لديهم تشوهات خلقية بين متلازمة داون في محافظة دهوك.

Introduction

Down syndrome (DS) is the most common autosomal chromosomal aneuploidy in human and the best known of all malformation syndromes associated with developmental delay, mental retardation and several characteristic physical features [1,2]. In addition, people with DS have an increased risk for Congenital Heart Diseases, leukemia, gastro interstitial tract abnormalities, immunological impairments, and Alzheimer disease [3].

The birth prevalence of DS is approximately 1 in 650-1000 live-born children world-wide which make the syndrome the most common cause of mental retardation [4].

Generally, DS can be caused by three types of chromosomal abnormalities: trisomy 21 (non-disjunction), translocation, or mosaicism. More than 95% of DS individuals have trisomy 21 which results from non-disjunction error during gameto-genesis in chromosome 21. About 2-4% results from a translocation of chromosome 21, while only 1-2% is mosaicism that showing a normal cell line additionally to trisomy [5]. Mosaic DS individuals may be phenotypically less severely affected than Individuals in trisomy or translocation, but their conditions are indistinguishable in all other aspects [6].

Down syndrome due to non-disjunction is typically not inherited. Mosaic DS is also not inherited, but is the result of random error during cell division, resulting in some cells having an extra copy of the chromosome. Translocation DS may be inherited [7].

Down syndrome is associated with variable phenotypes. However, mental retardation, neonatal hypotonia, hypocellular brain and minor facial dysmorphic features such as small nose, upslanting palpebral fissures, speckling of iris (Brushfield spots), wide gap between the first and second toes, flat facial profile, low set ears, single palm crease and shortened 5th finger can be seen in almost all individuals with DS [8].

In addition, individuals with DS are at an increased risk for several congenital anomalies and some health problems such as congenital heart defects, Leukemia, Alzheimer's disease, Hypothyroidism and Gastrointestinal track anomalies [9,10]. But these Individuals are different in their health situations, not every person will suffer serious health problems. Many of associated conditions and health problems can be treated with surgery, certain medications or some interventions [11].

Cytogenetic investigation is an important technique to confirm clinical diagnosis and to determinate the recurrence risks of DS [12].

The purpose of this study was to found the proportion of chromosomal abnormalities in patients with Down syndrome in Duhok province, as well as to study their clinical features.

Materials and Methods

The current study was performed according to the cross-sectional descriptive study design.

A total of 86 Individuals with DS for cytogenetic analyses were collected from Hivi pediatric hospital in Duhok city and Awat institute for mental retardation children from October 2014 to April 2015. Cytogenetic analyses and karyotyping foe each individual was performed at the scientific research Centre in the College of medicine, University of Duhok. All patients were subjected to full clinical, laboratory examinations.

Before working, permission of Ethics Committee and permission from all children parents had been taken.

A questionnaire form was filled for each patient that included sociodemographic characteristics of individuals and their

mothers, comorbidity, recurrent infections and Clinical features. The information's about congenital heart disease has been taken from individual profiles in Hivi Hospital and Awat institute.

All steps for preparation of chromosome from lymphocytes cultured of peripheral blood and all solutions needed prepared according to Rooney [13].

Chromosomal culture was carried out by 1ml of peripheral whole blood collected in sodium heparinized tube each patient then added to a flat culture tube that containing 10ml of RPMI1640\L-glutamine, 2ml of fetal bovine serum, 200µ of Phyto-haemagglutinin (10 µg/ml), 200µ penicillin-streptomycin solution (10 µg/ml).

After 72 hours of incubation at 37°C, 100µ of Colcemid was added, after 60 minutes, the cells were harvested by centrifugation 1500/rpmi for 7 min. Then, 10ml of 0.075M KCl solution was added and mixed and incubated at 37°C for 30 min. After centrifugation 1500/rpmi for 7 min, hypotonic supernatant was removed. Then, 10ml of cold, fresh fixative solution (3:1 methanol: glacial acetic acid) was added drop by drop for the first 2 ml to the cell pellet. Centrifugation was done afterward, and the supernatant was removed, last step was repeated until a clear pellet was obtained. Finally, cells obtained were dropped on clean distinct slides, staining with Giemsa stain.

Slides were examined and analyzed with bright field microscope using BX51 Olympus microscope and karyotyping were performed with the aid of computer based karyotyping system (Cytovision version 7.2 from Leica microsystem). At least 15-20 metaphase spread Captured by using a satellite capture station and the images transferred to an image analyser. For each patient 15-20 cells were counted and analyzed and finally designated the karyotype according to the ISCN (1995).

After completing karyotyping, data analysis was performed by using IBM SPSS Statistics software version 22. Descriptive data were presented for continuous variables as mean ± SD, while qualitative data description done by calculating number and percentage. t-test was used to compare between two means and Chi-square (x2) tests was used to compare between proportions, P value $\leq$ 0.05 considered statistically significant.

Results

All 86 cases included in this study were cytogenetically confirmed cases with a clinical diagnosis of Down syndrome, 37 (43%) were males and 49 (57%) were females with male to female ratio of 1:1.3 and the age of the enrolled patients ranged from 1 day to 35 years with a median age of 6.1 years (mean 8.3±7 years).

The maternal ages at the time of delivery of index babies were ranged from 21 years to 47 years with a median age of 33 years (mean 32±5.8) and out of 86 DS individuals, 30 (34.9%) were born to mothers ≥35 years of age, while 56 (64.1%) were born to mothers ≤35 years of age. Also 31 (36.2%) mothers of affected child gave history of abortion, and majorities have 1-2 abortion and occasionally more than 2 abortions

The orders of affected individuals were from 1stto 14th, the 3rdorder was the most common order constituting 14 (16.3%) individuals with DS. Consanguinity relationship showed that 44 (51.2%) couples were in a consanguinity relationship and 42 (48.8%) had no consanguinity.

The cytogenetic results of the analysis of 86 cases of DS listed in table I, showed that the in Trisomy 21 was the most common type of abnormality detected in 79 (91.9%) of the cases, while there were 5 (5.8%) cases of Translocation and 2 (2.3%) cases of Mosaicism. These various karyo-gramsare shown in figures 1 and 2.

Frequencies of clinical features listed in Table II, It shows that the craniofacial abnormalities comprised epicanthic folds was the most common feature among DS cases presenting in 69 (80.2%) cases, Upslanting palpebral fissures In 61(70.9%) cases, protruding tongue in 58 (67.4%) cases, short broad hand in 49 (57%) cases. On the other hand excessive skin folds on

neck were the least common feature which only presented in 21 (24.4%) cases.
About clinical complications, Congenital heart defect presented in 23 (26.7%) of cases, Hypothyroidism presented in 9 (10.5%) cases and under developed genitalia presented in 7 (8.1%) cases.

Table 1: Cytogenetic results patients with in Down syndrome.

Cytogenetic Results	Frequency	%
Trisomy 21		
47,XY,+21	35	40.7%
47,XX,+21	44	51.1%
Translocation		
46,XX,t(14;21)	2	2.3%
46,XY,t(14;21)	2	2.3%
46,XX,t(1;21)	1	1.1%
Mosaic		
[46,XX/47,XX,+21]	2	2.3%
Total	86	100%

Table 2: Frequencies of clinical features in Down syndrome

Clinical Features		Frequency	%
Hand and Foot	Short broad hands	49	57%
	Simian crease	48	55.8%
	Clinodactyly (Incurved finger)	25	29.1%
	Plantar furrow	35	40.7%
	Sandal gap*	55	64%
Head	Epicanthic folds	69	80.2%
	Upslanting palpebral fissures	61	70.9%
	Open small mouth, protruding tongue	58	67.4%
	Furrowed tongue	36	41.9%
	Depressed nasal bridge	54	62.8%
	Low set, small ears	49	57%
	Microcephaly	42	48.8%
	Hypertelorism**	33	38.4%
	High arched palate	25	29.1%
	Short neck	43	50%
	Excessive skin folds on neck	21	24.4%

* Sandal gap: Gap between 1st and 2nd toe;
** Hypertelorism: increase in the interorbital distance

Table 3: Clinical complications among Down syndrome individuals.

Clinical complications	Frequency	%
Developmental delay	33	38.4%
Congenital heart defect:	23	26.7%
Hypothyroidism	9	10.5%
Under developed genitalia, Small penis	7	8.1%
Brushfield spots (Iris)	3	3.5%

Table 4 (A, B, C) shows demographic features, clinical features, and Co-morbidities among different cytogenetic groups of DS detected in the current study.

Table 4 (A): Demographic features among different cytogenetic groups of Down syndrome.

Demographic features	Trisomy	Translocation	Mosaicism
Cytogenetic Results	(79 cases)	(5 cases)	(2 cases)
Age of DS	Mean (8.1±6.7)	Mean (6.2±5.9)	Less than 1 year 6 year.
Sex	35M:44F	2M:3F	0M:2F
Order in Family	Mean (7±3)	Mean (4±2)	10th 14th
Maternal Age	Mean (32.7±5.7)	Mean (31.2±4.6)	40 year 45 year
Abortion	36.7%	40%	0%
Consanguinity	41 (51.9%)	2 (40%)	1 (50%)

Table 4 (B): Clinical features among different cytogenetic groups of Down syndrome.

Clinical features		Trisomy (79 cases)	Translocation (5 cases)	Mosaicism (2 cases)
Hand and Foot	Sandal gap:	51(64.6%)	3(60%)	1(50%)
	Short broad hands	45 (57%)	4 (80%)	0(0%)
	Simian crease	44(55.7%)	3(60%)	1(50%)
	Clinodactyly	22(27.9%)	2(40%)	1(50%)
	Plantar furrow	32(40.5%)	2(40%)	1(50%)
Head	Epicanthic folds	63(79.8%)	5(100%)	1(50%)
	Upslanting Palpebral fissures	57(72.2%)	3(60%)	1(50%)
	Open small mouth, Protruding tongue	53(67.1%)	3(60%)	2(100%)
	Depressed nasal bridge	49(62.0%)	4(80%)	1(50%)
	Low set, small ears	43(54.4%)	5(100%)	1(50%)
	Microcephaly	38(48.1%)	3(60%)	1(50%)
	Short neck	37 (46.8%)	5(100%)	1(50%)
	Furrowed tongue	32(40.5%)	3(60%)	1(50%)
	Hypertelorism	28(35.4%)	4(80%)	1(50%)
	High arched palate	21(26.6%)	3(60%)	1(50%)
	Excessive skin folds on neck	19(24.1%)	1(20%)	1(50%)

Table 4 (C): Co-morbidities among different cytogenetic groups of Down syndrome.

Co-Morbidity features	Trisomy (79 cases)	Translocation (5 cases)	Mosaicism (2 cases)
Developmental Delay	27(34.2%)	5(100%)	1(50%)
Congenital heart defect:	21(26.6%)	1(20%)	1(50%)
Hypothyroidism	^(10.1%)	·(0%)	1(50%)
Under developed genitalia, Small penis	5(6.3%)	2(40%)	0(0%)
Brushfield spots (Iris)	3(3.8%)	0(0%)	0(0%)

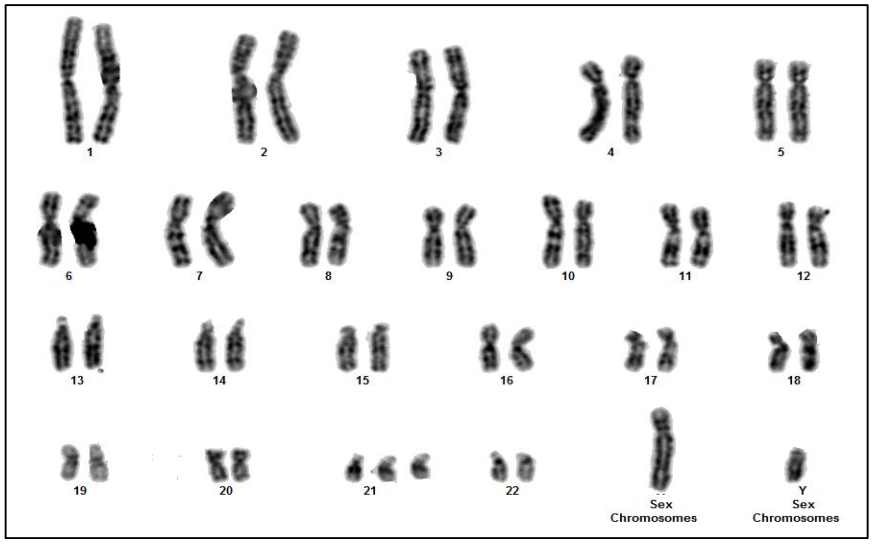

Figure 1: Karyogram of Trisomy 21 (47,XY,+21).

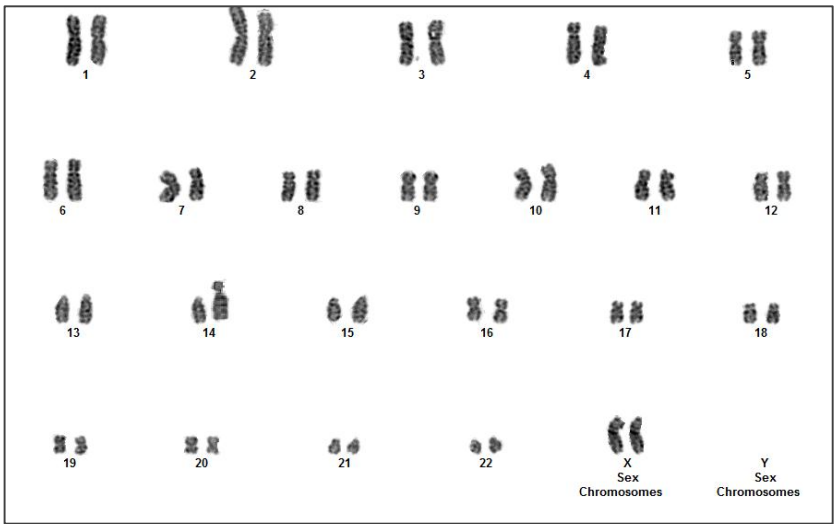

Figure 2: aryogram of Robertsonian translocation between chromosomes 14 and 21 [46,XX,t (14;21)].

Discussion

Several factors had been claimed to be associated with increased incidence of DS including: advanced maternal age, birth order of the affected children, consanguinity, and number of maternal miscarriage [14-16].

Down syndrome frequently encountered in our area with 1/960 being affected and this figure somewhat similar to that reported from Malaysia, Egypt and Germany [17-19], higher than United states, Singapore, England and Wales [20-22], but lower than India, most Arab countries, Iran and South Africa [23-25,5] and this mostly related to cultural factors as multiparity and probably exposure to environmental pollution including radiation.

Ages of the enrolled patients ranged from 1 day to 35 years with a mean of 8.3±7.6 years (Median 6.1 years) and this figure is slightly higher than many international studies as about 46 enrolled patients were already diagnosed clinically and they were registered at Awat institute for mental retardation and because of the absence of routine cytogenetic techniques for such disorders. El-Gilany *et al* [26] reported a mean age of diagnosis of 12.2 months among 712 Egyptian DS individuals, Azman *et al* [19] reported a mean age of diagnosis of 10.6 months among 149 Malaysian DS individuals and Kava [27] reported a mean age of diagnosis of 18 months among 524 Indian DS individuals. Al-Harasi [28] reported almost 90% of 680 cases of DS children born in Oman were diagnosed cytogenetically within 6 months after birth.

Females are predominant in the current study with sex ratio of (M:F =1:1.3) and this is relatively compatible with the data from small numbers of patients from Jordan which was (M:F =1:1.2) [29] but different to most other results from the region including that previously done in Duhok city based on clinical features only which was 1.5:1 [30]. Mehdipour [24] reported sex ratio of 1.5:1 in 150 Iranian DS individuals, El-Gilany *et al* [26] reported sex ratio of 1.14:1 among 712 Egyptian DS individuals and Frennyin [31] reported sex ratio of 2.3:1 among 382 Indian DS individuals.

In spite of decades of research, the variability sex distribute in DS individuals is still unclear. Several hypotheses have been discussed, such as not-optimal timing of insemination in relation to ovulation [32], the joint segregation of chromosome 21 with the Y chromosome in spermatogenesis or chromosomal non-disjunction during meiotic division of oogenesis which is caused by Y chromosome-bearing spermatozoa [33-35] Affection of female more frequently in the current study remained unclear.

The mean maternal age for DS individuals in our study was 32±5.8 years, which is slightly but significantly lower from the 34.4 years age in Western countries [36,37], this indicates that there is a clear effect of advanced maternal age on the DS birth prevalence in Duhok province and this difference may be related to younger age at marriage in our region or underestimation of maternal age as the females do not mention their real ages correctly.

Down syndrome mostly observed among multiparous women with the birth order of second, third and fifth birth order and particularly the 3rd order. When individuals were stratified by karyotypes, mosaic DS were significantly associated with higher parity and these results are relatively compatible with data of few studies in Egypt, Iran and India [38,16,39].

On the other hand, Murthy *et al* [25] reported that an individual with DS were mostly the last one or second last one. Several studies suggest that there is an increasing risk with increasing parity as Doria-Rose *et al* [40] suggested that higher parity is associated with an increased risk of giving birth to a DS child, both for women aged more than 35 years and for women under 35 years of age, while Chan *et al* [41] reported that there is no increased risk noted with increased parity.

It has been suggested that the consanguinity among parents of DS individuals is associated with the higher rate of DS in some Arab countries including Iraq [15]. Consanguineous marriages are favored by the Kurds and Arab communities in the

Middle East especially the first cousin marriages due to some social and economic reasons and to maintain the family properties [42]. Increased consanguinity rate of DS parents as compared to the general population was observed in the current study (51.2%) and those data are comparable to that reported from Oman [43] and this may be due to a higher probability of carrying rare recessive alleles influencing non-disjunction that could result in an increased aneuploidy rate of the progeny specially in the younger aged mothers [44,45] or recessive genes, possibly preventing the loss of the trisomy 21 fetus [46,47].

Miscarriage was observed with higher rate among mothers of DS children in the current study (36.2%) in comparison to the general population (14.3%) [48] and this may be due to inherited risk for chromosomal aneuploidy that commonly ended with abortion in the previous pregnancies [14]. Also abortion rate was higher than most other studies at 8.6% [28] and this might be due to higher rate of abortion in the region [48].

Regarding clinical profiles, craniofacial features considered to be the most important indicators of clinical suspicion of DS [49]. Among the craniofacial features studied in the current study, epicanthic fold was the most frequent feature observed in 69 (80.2%) cases, which is compatible with the study of Erika *et al* [12]who reported it in (79%) among DS individuals in southeast of Brazil, but this was quite different from that reported from southeast Asia with prevalence of only (17.5%) from northeast Malaysia and (59.6%) from India [27,19].

The major five clinical features present in more than 60% of the total cases were the epicanthic fold, upslanting palpebral fissures, protruding tongue, sandal gap and depressed nasal bridge which are comparable to the other studies in Table 5.1.

Regarding complications and associated co-morbidities, congenital heart defect was encountered in 23 (26.7%) cases and this figure was smaller than that previously reported by Garjess and Muhsin [30] in Duhok province who reported CHD in 44 (55%) out of 80 cases with DS and this mostly due to inclusion of older patients from Awat institute and randomly selected patients from different region of Duhok who lack CHD and survived longer than those who suffered from CHD and pass away in the early childhood. The figure was also lower than that reported from Brazil, Malaysia and India (49%, 56% and 49% respectively) [19,12,50] and mostly due to the same reason mentioned above.

Thyroid dysfunction observed more frequently (10.5%) among enrolled patients with DS than general population at 0.13% as revealed from the recent study from Duhok and these data are in concordance with other studies which all show higher prevalence of thyroid dysfunction among DS patients [51,50]. About 15% of adolescents with Down syndrome are hypothyroid, and there is evidence for a steady decline in thyroid function as age increases [52]. Hypothyroidism was significantly more frequent among non-disjunction individuals in comparison to those with translocation.

Table 5-1: Comparison of clinical features in Down syndrome individuals

Dysmorphic feature	Duhok, Iraq (Current study %)	Malaysia [19]	Brazil [12]	India [27]
Epicanthic folds	80.2%	17.5%	79%	56.9%
Upslanting Palpebral fissures	70.9%	89.3%	-	83.9%
Protruding tongue	67.4%	19.2%	33.9%	29.9%
Sandal gap:	64%	33.3%	64.5%	46.2%
Depressed nasal bridge	62.8%	64.9%	93.5%	50.9%
Short broad hands	57%	-	78.7%	-
Low set, small ears	57%	56.1%	32.3%	66.9%
Simian crease	55.8%	36.8%	83.9%	33.2%
Short neck	50%	-	83.9%	-
Microcephaly	48.8%	-	60.7%	-
Furrowed tongue	41.9	-	-	-
Plantar furrow	40.7%			
Hypertelorism	38.4%	33.3%	72.6%	33.9%
Clinodactyly	29.1%	19.2%	46.7%	36.8%
Excessive skin folds on neck	24.4%	12.2%	-	36.8%
High arched palate	29.1%%	-	-	

Cytogenetic analysis of all enrolled individuals revealed that trisomy 21 were the most common (91.9%) followed by translocation (5.8%) and mosaicism (2.3%) and these are of the same order of magnitude as reported from most other studies. Table 5.2 reveals the data of the current study in comparison to different other studies.

The Data from this study showed that the frequency of trisomy 21 (91.9%) is relatively compatible with the data from Czechoslovakia and Brazil at 91.7% and 92.2% respectively [53,54], while it is lower than the data from Moroccan, Egypt and Malaysia at 96.2%, 95.4% and 94.6% respectively [40,19] and greater than that reported from Indian and Iran at 83.2%, and 88% respectively [24,5]

Table 5-2: Numbers and frequencies of different karyotype patterns in Down syndrome reported in this study and data from worldwide surveys.

Source	Total No.	Trisomy		Translocation		Mosaicism		Ref.
		No.	%	No.	%	No.	%	
Duhok, Iraq	86	79	91.9	5	5.8	2	2.3	Current study
Jordan	33	28	84.4	3	9	2	6	[29]
Czechoslovakia	109	102	91.7	5	4.5	2	1.8	[51]
Malaysia	149	141	94.6	1	0.7	7	4.7	[19]
Iran	150	132	88	1	0.6	17	11.3	[24]
Albanian	305	285	93.4	17	5.6	3	0.9	[55]
Brazil	387	357	92.2	24	6.2	6	1.5	[52]
Egypt	673	642	95.4	18	2.7	5	0.7	[40]
Oman	680	640	94.1	20	2.9	19	2.8	[28]
India	1020	855	83.2	51	5	110	10.8	[5]
England and Wales	5,737	5,411	94.3	220	3.8	66	1.2	[21]

As shown in Table 5.2 the frequencies of translocation varied from (0.6%) to (9%) while the frequencies of mosaicism varied from (0.5%) to (11.3%). In general, all studies observed that the frequency of nondisjunction was very much higher than the frequency of mosaicism and translocation.

Although real comparison among different cytogenetic groups is subjective due to small numbers of translocation and mosaic Down individuals, however, in comparing different cytogenetic groups: birth order of the index individual tends to be higher among mosaic DS children in comparison to other cytogenetic groups and mosaic DS associated significantly with older maternal age at the delivery of the index DS patients. History of abortion among mothers of DS individuals tends to be significantly higher among mothers of trisomy and translocation DS than mothers of mosaic DS individuals. Paternal consanguinity was not different among the three groups and these data are comparable to that reported from Egypt [26].

Regarding clinical manifestation, the most consistent features among trisomy individuals were the epicanthic folds, upslanting palpebral fissures and sandal gap, while the most features associated with translocation were epicanthic folds, small ears, Hypertelorism and short broad hands. In Mosaicism protruding tongue was the most common features, while all other features have an equal frequency.

Clinical complications like developmental delay were significantly more frequent in translocation than trisomy and absent in mosaicism and on the other hand hypothyroidism was more common among trisomies and these are quite different from that reported from United Kingdom that show equal percentage of developmental delay and hypothyroidism among trisomies and translocation [56], but somewhat similar to that reported from Egypt with higher prevalence of hypothyroidism among trisomies [26].

Finally as comparable to data reported from Baghdad [57] no significant difference found among different cytogenetic groups regarding frequency of congenital heart diseases.

Conclusion

1. This study is a first record of cytogenetic analysis and karyotyping for Down syndrome individuals in Duhok province, Iraq.
2. Nondisjunction of Trisomy 21 was the most common karyotype followed by translocation and mosaicism. Down syndrome among Duhok province population was more frequent in females than males.
3. A high rate of consanguinity has been reported among parents of children

with Down syndrome. Among the craniofacial features studied, epicanthic fold was the most frequent, while excessive skin fold on neck was the least common.

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