# Clinical and Cytogenetic Profile of Down Syndrome at King Hussein Medical Centre

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## ABSTRACT

**Objective:** To describe the cytogenetic pattern, clinical features and other systemic anomalies of patients with Down syndrome at King Hussein Medical Centre.

**Methods:** Retrospective analysis of medical case files of Down syndrome patients attending the Genetics Clinic at King Hussein Medical Center was performed. A total of 87 patients were studied during the period between June 2007 to December 2009 (54 males and 33 females; M:F ratio 1.6:1). The following information was recorded: age at presentation; gender; maternal age; craniofacial and other physical features; presence and type of congenital heart disease, gastrointestinal abnormalities, hearing assessment, ophthalmic evaluation, complete blood count, kidney and liver function tests, thyroid function tests, and results of cytogenetic evaluation

**Results:** Out of the 87 patients studied; ophthalmologic abnormalities were detected in 20 out of 67 patients whose eye examination was available. Congenital heart disease was found in 41 (48.8%) cases out of 84 patients who underwent Echocardiographic examination. Gastrointestinal anomalies were noted in 9 (11%) cases. Hypothyroidism was present in 17(22.7%) cases out of 75 patients. Results of chromosomal analysis were available in 80 patients and showed free trisomy (non-disjunction) in74 patients (92.5%), two (2.5%) had translocation, and three (3.8%) were mosaics and one patient (1.3%) had an additional chromosomal abnormality.

**Conclusion:** Down syndrome is associated with a significant systemic abnormalities and is frequently seen among mothers younger than 25 years of age. Early diagnosis and proper screening should be undertaken among these patients.

**Key words:** Down syndrome, Karyotype, Screening.

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## Introduction

Down syndrome is the most common autosomal trisomy, and is the most common genetic cause of severe learning difficulties. Its incidence ranges from 1 in 600 to 1 in 1000 in live-born infants.[1,2] There are no available figures of the incidence or prevalence of Down syndrome in Jordan but figures from Egypt showed that the incidence of Down syndrome has been reported to be 1 in 1000 births.[3]

Diagnosis of Down syndrome is usually suspected at birth because of characteristic phenotypic features but this can be difficult to ascertain and the diagnostic accuracy ranged from 100% in non-disjunction and translocation to as low as 37% of mosaic Down syndrome.[1] and this could be due to the fact that these patients may be phenotypically less severely affected than persons with non-disjunction or translocation.Therefore, chromosomal

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analysis is needed to confirm the diagnosis, to determine the risk of recurrence and for genetic counselling.

The objective of this study was to evaluate the cytogenetic pattern, clinical features and systemic anomalies in patients with Down syndrome who attend the genetics clinic at King Hussein Medical Centre (KHMC).

## Methods

Patients attending the genetics clinic at KHMC, Amman-Jordan, with the diagnosis of Down syndrome were enrolled in the study. Case medical files of these children were reviewed from June 2007 until September 2009, and the following information was recorded: age, gender, age at presentation; maternal age; craniofacial and other physical features; presence and type of congenital heart disease, gastrointestinal abnormalities, hearing assessment, ophthalmic evaluation, complete blood count, kidney and liver function tests, thyroid function tests, and results of cytogenetic evaluation.

A total of 87 patients were enrolled, age ranged from 20 days to 10 years; 54 were males and 33 were females, male to female ratio (1.6:1). Mean age +/- standard deviation of patients was 31.6 ± 30.2 months (range: 0.9 – 158 months).

Karyotyping was performed at Princess Iman Laboratory and Research Centre; out of the 87 cases enrolled, the results of chromosomal analysis were unavailable for 7 patients. Echocardiography and cardiac evaluation was done at Queen Alia Heart Institute and the results were available for 84 patients. Results of thyroid function tests were available for 75 patients. Ophthalmic evaluation was available for 67 patients whereas hearing assessment was available for 69 subjects.

## Results

Mean maternal age at birth of the affected child was 33.8 ± 7.2 years (range: 18-48 years).

Maternal age categories showed 10 mothers were less than 25 years, 35 mothers were between 25 and 35 years, and 42 mothers were over 35 years of age.

Out of the 80 patients with available karyotype 74 (92.3%) had non-disjunction, 2 (3.1%) had translocation, 3(4.6%) were mosaics, and one patient (1.3%) had an additional chromosomal abnormality which was 48, XXY+21. The mother age groups for these patients showed 9 mothers less than 25 years of age, 31between 25 and 35 years of age, and 40 were more than 35 years, Table I.

Congenital heart disease was present in 41 (48.8%) out of 84 patients with available echocardiographic reports, 12 had Atrial Septal Defect (ASD), 8 had ASD and Ventricular Septal Defect (VSD), 7 had atrriventricular canal (AV canal), 3 had Patent Ductus Arteriosus (PDA), one; coarctation of aorta, 10 had other combinations of heart defects.

Otolaryngeal and hearing evaluation showed impaired hearing in 35 out of 69 patients screened. Conductive hearing loss was present in 16 patients, and absent otoacoustic emissions was seen in 19 of subjects.

Opthalmological abnormalities were found in 20 out of 67 cases and included refractive errors 6, squint 4, nystagmus 2, brushfield spots were seen in only one patient and 7 patients had other abnormalities.

Gastrointestinal anomalies were found in 9 (10.3%) cases out of 87 patients, two had diaphragmatic hernias, two had inguinal hernias, three had gastoeosophegeal reflux, one had duodenal atresia and another one had celiac disease which was proved by duodenal biopsy and serology. None of our patients had Hirschsprung disease or anorectal abnormalities.

Regarding thyroid function, 17 out of 75 patients whose thyroid function tests were available had hypothyroidism.

Complete blood count showed mild anaemia in 5 cases, one had transient myeloproliferative disease, two had transient neutropenia and 5 had neonatal polycythemia.

Liver function tests and blood chemistry showed hypocalcemia and hypomagnesemia in one patient who had convulsions, 3 patients had prolonged jaundice.

The karyotype pattern in this study showed that out of the 80 patients with available karyotype, free trisomy (non-disjunction) was seen in 74 patients (92.5%), two (2.5%) had translocation, and three (3.8%) were mosaics and one patient (1.3%) had an additional chromosomal abnormality which was 48, XXY+21, Table II, parents of the two patients with translocation had normal karyotype which means that the translocation was not inherited in their cases.

## Discussion

Down syndrome is relatively a common disorder in paediatric practice. However, its incidence greatly increases among children born to mothers over 35 years of age. The rise in average maternal age could

**Table I.** Mother age categories and karyotype

| Karyotype | Mother age categories | | | Total |
|---|---|---|---|---|
| | < 25 years | ≥25-35 years | >35 years | |
| Nondisjunction | 7 (8.8%) | 29 (36.3%) | 38 (47.5%) | 74 (92.5%) |
| Translocation | 0 (0%) | 2 (2.5%) | 0 (0%) | 2 (2.5%) |
| Mosacism | 2 (2.5%) | 0 (0%) | 1 (1.3%) | 3 (3.8%) |
| Others | 0 (0%) | 0 (0%) | 1 (1.3%) | 1 (1.3%) |
| Total | 9 (11.3%) | 31 (38.8%) | 40 (50%) | 80 (100%) |

**Table II.** Karyotype frequencies in different countries

| Source | Author | Total No. | Non-disjunction | Translocation | Mosacism | Nonclassic |
|---|---|---|---|---|---|---|
| Current study | Amayreh *et al* 2009 | 80 | 74 (92.5%) | 2 (2.5%) | 3 (3.8%) | 1 (1.3%) |
| Malaysia | Azman *et al* 2007[5] | 149 | 141 (94.6%) | 1 (0.7%) | 7 (4.7%) | 0 |
| Ireland | Devlin 2004[1] | 208 | 197 (94.7%) | 3 (1.45%) | 8 (3.85%) | 0 |
| Egypt | Mokhtar *et al* 2003 [3] | 673 | 642 (95.4%) | 18 (2.7%) | 5 (0.7%) | 8 (1.2%) |
| England and wales | Mutton *et al* 1996[20] | 5737 | 5411 (94.4%) | 220 (3.8%) | 66 (1.2%) | 40 (0.7%) |
| England | English *et al* 1989[21] | 65 | 63 (96.9%) | 1 (1.5%) | 1 (1.5%) | 0 |

bring with it an increase in the number of pregnancies affected by Down syndrome as shown by a study carried out in Europe which showed more than twofold increase in total prevalence of Down syndrome in certain regions with the increasing proportion of "older" mothers.[4]The mean maternal age at birth of the affected child in our study was 33.8 ± 7.2 years (range: 18-48 years) which was comparable with mean maternal age in other studies.[3,5] Although a study by Kava MP et al in India showed that the mean maternal age at birth of the affected child was 26.8 years.[6] Maternal age categories showed 10 mothers were less than 25 years, 35 mothers were between 25 and 35 years, and 42 mothers were over 35 years of age. Out of the 80 patients with available karyotype, the mother age groups for these patients showed 9 (11%)mothers less than 25 years of age, 31(39%)between 25 and 35 years of age, and 40 (50%)were more than 35 years, Table I shows a higher percentage in older mothers which is similar to other studies.[3,4]

The clinical diagnosis of Down syndrome in the neonatal period usually doesn't present a significant difficulty, although the variable nature of the presenting features can make the diagnosis uncertain, and the diagnostic accuracy on clinical grounds was found to be around 70% by Hindley.[7] Therefore karyotyping should be performed whenever there is a clinical suspicion of Down syndrome in a newborn. In our study the physical signs were as follows; 82% had upwards and outwards slanting eyes, 72% had increased skin at nape of neck, 59% had abnormal hand creases, 55% had hypotonia, 47% had brachcephaly, whereas 38% had the so called wide sandal gap.

Children with Down syndrome have multiple systemic abnormalities in addition to mental impairment, they have an increased risk of congenital heart disease, gastrointestinal anomalies, thyroid disease, hearing and visual disorders, obstructive sleep apnea, acquired hip dislocation and leukaemia.[8]

Congenital heart disease is particularly common in these children, in this study, 41 patients were found to have congenital heart disease out of 84 patients with available echocardiographic reports; 12 had ASD, 8 ASD VSD, 7 AV canal, 3 PDA, 1 coarctation Aorta, 10 had other combinations of heart defects. And this is similar to figures from

other studies.[5,9] although a study from Sudan showed markedly higher figures of congenital heart disease.[10]

Regarding otological disorders, these children usually have higher incidence of hearing problems; middle ear effusion, impacted wax, otitis media, and conductive hearing loss.[8,11]

Opthalmological abnormalities are more frequent in these children especially refractive errors and strabismus.[12,13] Twenty patients in this study out of 67 cases whose ophthalmic assessment was available showed ophthalmic abnormalities which included; refractive errors 6, strabismus 4, nystagmus 2, brushfield spots were seen in only one patient and 7 patients had other abnormalities.

Altered thyroid function is common in patients with Down syndrome especially hypothyroidism which usually has subtle presentation and can be particularly challenging to detect in these patients because of the symptoms of hypothyroidism may overlap with features of Down syndrome.[14,15]

Infants with Down syndrome, especially boys, showed elevated levels of TSH at neonatal screening, indicating the occurrence of mild hypothyroidism already in early life, the TSH levels may not predict development of manifest thyroid disease later in childhood.[16]

Seventeen (22.7%) out of 75 patients whose thyroid function tests were available had hypothyroidism which is similar to international figures.[17,18] Popova *et al* has shown that there is no female predominance in thyroid disease in Down syndrome patients.[19] which contrasts with the fact that females usually outnumber males in thyroid disease in the general population. The male to female ratio in our patients who had hypothyroidism was (1.4:1), 10 were males and 7 were females which show rather male predominance.

## Conclusion

Down syndrome is associated with a significant systemic abnormalities and is frequently seen in mothers younger than 25 years of age. Early diagnosis and proper screening should be undertaken among these patients. Follow up and management should preferably be undertaken by a team with special experience in managing these cases because of the high association of this condition with systemic abnormalities.

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