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The Features of Down Syndrome and the Risk of Parent's Age

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Authors' contributions

This work was carried out in collaboration among all authors. All authors read and approved the final manuscript.

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Original Research Article

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ABSTRACT

Background: Down syndrome is the most common autosomal disorder in humans. And the most common genetic chromosomal disorder causing mental disability in children.
It also cause other medical abnormalities including heart and gastrointestinal disorder.
These children sharing common features and characteristic faces.
Each individual with this syndrome will not have all the features, but they will have a unique combination.
Objective: In our study we try to spot light on the craniofacial features of Down syndrome in our country: their percentage; to compare it with another study in other countries.
We also focus on the craniofacial features accuracy in diagnosis. Karyotyping not always available.
Also we study the risk factors where we found that the mother age is not the only risk factor, but also the father age play a big role in Down syndrome and this risk factor needs to be studied with large number of patients.
Also we study the problems associated with Down syndrome and its percentages, and to compare it with other study done in our neighbor's countries, where we found many differences
Setting and Design: Our study is a descriptive, case series retrospective study was conducted in Benghazi Libya's children hospital.
This study includes 73 patients who were referred to our Genetic clinic from October 2016 to march 2017.
The genetic clinic is the only clinic in Benghazi and the whole East of Libya.

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This clinic follows children with DS and children with dysmorphic features in Benghazi and the Libyan 'east.

Materials and Methods: We studied 73 children randomly from different age group, and different socioeconomic classes, who attend the genetic clinic, which is an outpatient clinic and the only clinic which follows children with DS and dysmorphic feature in a pediatric hospital in Benghazi-Libya.

We took the history from the parent (the father and the Mother).
The investigation done in our hospital.
Father and mother age at pregnancy.
Spontaneous or induced pregnancy.
Drug history of the mothers and fathers.
History of abortion and normal children.
Any other baby with Down syndrome or other dysmorphic features.
Echocardiography done for all children.
Ultrasound abdomen and brain did for all children.
Thyroid function test done for all children and repeated annually for all children.
The diagnosis done mainly by clinical features. Some cases (40 cases) are proved by karyotype chromosomal analysis.

Keywords: Down syndrome; autosomal disorder; genetic chromosomal disorder; karyotype.

1. INTRODUCTION

Down syndrome is the most common autosomal disorder in human. And the most common genetic chromosomal disorder causing mental disability in children.

It also cause other medical abnormalities including heart and gastrointestinal disorder.

These children sharing common features and characteristic faces.

Each individual with this syndrome will not have all the features, but they will have a unique combination.

Little about DOWN SYNDROME (D.S).

In 1862 an English physician john Langdon Down 1st characterized DS as a distinct form of mental disability [1,2].

The cause of which was not known until 1959 where it was showed that this individual carried 47 chromosomes instead of 46 [1].

The extra chromosome labeled as the 21st and the condition as trisomy 21.

The condition was referred to as mongolism till 1965 when the WHO dropped this reference after a request by Mongolian delegate.

And they supported Down syndrome [1].

DS is the most common autosomal disorder in human [3].

It occurs in all areas of the world and among all racial groups

The typical humane karyotype is designed as:-

46, XX typical for human female and

46, XY typical for human male [1].

1.1 What is Trisomy?

It is a chromosomal anomaly that is characterized by the presence of an extra chromosome in the cells of a person's body.

DS occur in approximately 1 in 700 of all live births.

However the incidence varies with the age of mother, the incidence for mother aged 25 years is 1 in 1400 and increases to 1 in 40 for mother aged 45 years [4].

1.2 Genetics of the Disease

The most common cause of having a DS babies is presence extra copy chromosome 21 resulting in trisomy. Non disjunction type ~95% of all cases.

The other causes can be Robertsonian translocation and isochromosomal or ring chromosome.

Ischromosome is a term used to describe a condition in which two long arms of chromosome separate together rather than the long and short arm separating together during egg sperm development [5,6].

Trisomy 21 (karyotype 47, XX, + 21 for females and 47, XY, + 21 for males) is caused by a failure of the chromosome 21 to separate during egg or sperm development [5].

In Robertstonian translocation which occurs only in 2-4% of the cases, the long arm of the chromosome 21 is attached to another chromosome (generally chromosome 14) [5].

The extra chromosome can attached to another chromosome usually chromosome 13, 14, 15, 21 and 22. With total number 46 chromosome [4].

Translocations account for 9% of the children with DS born to mothers under the age of 30 years [7].

The phenotype in translocation DS is not distinguishable from the regular trisomy 21DS [7].

While mosaicism deals with the error or misdivision that occurs after fertilization at some point during cell division.

Due to this people with mosaic DS have two cell lineages that contribute to tissues and organs of individuals with Mosaicism (one with the normal number of chromosomes, and other one with an extra number 21 [5,2].

The percentage of trisomic cells may vary between cells located in different parts of an individual's body.

For example, the percentage of trisomic cells in the muscles may be different from that seen in the brain cell or blood cells.

1.3 Features of Down Syndrome

Various conserved features are occurring in all DS populations, including learning disabilities, craniofacial abnormality and Hypotonia in early infancy [8].

DS individuals have variety of physical characteristics like a small chin, up slanted eye, poor muscle tone, a flat nasal bridge, a single crease of the palm and a protruding tongue due to a small mouth and large tongue [9].

Other features of Down syndrome;-

Each individual with DS will not have all the features seen in these children, but they have a unique combination,

The most common features are;-

Characteristic facial appearance.
Mild to moderate mental retardation.
Congenial heart disease.
Gastrointestinal problems.
Increased cold and respiratory problems.
Leukemia and Alzheimer.

2. MATERIALS AND METHODS

We studied 73 children randomly from different age group, and different socioeconomic classes, who attend the genetic clinic, which is an outpatient clinic and the only clinic which follows children with DS and dysmorphic feature in a pediatric hospital in Benghazi- Libya.

This study is a descriptive case series study, stated October 2016 and finished March 2017. We toke the history from the parent (the father and the Mother).

The investigation done in our hospital.

Father and mother age at pregnancy.

Spontaneous or induced pregnancy.

Drug history of the mothers and fathers.

History of abortion and normal children.

Any other baby with Down syndrome or other dysmorphic features.

Echocardiography done for all children.

Ultrasound abdomen and brain did for all children.

Thyroid function test is done for all children and repeated annually for all children.

The diagnosis done mainly by clinical features. Some cases (40 cases) are proved by karyotype chromosomal analysis.

3. RESULTS

Regarding the pregnancy and the family history;-

Almost all the mother have spontaneous pregnancy, only two mothers use CLOMID to get pregnant.

One family had 3 children with DS and no normal children,

One family have two children with DS, and three normal children

One family had one child with neurofibromatosis part of twin with Down syndrome.

One family had twin one normal child and one Down syndrome.

On examination, we found;-

1-Sex differentiation as follows

gender

		Frequency	Percent
Valid	male	41	56.2
	femal	32	43.8
	Total	73	100.0

56.2% was male
43.8%was females

2-clinical features as follows;-

Upper slanting eyes seen in 72 cases 98.6%
Depressed nose seen in 70 cases 95.8%
Sandal signs seen in 58 cases 79.4%
Brachycephaliy seen in 55 cases 75.3%
Microcephaly seen in 52 cases 68%
Simian creases seen in 47 cases 62%
Open mouth seen in 27 cases 37%
Protruded tongue seen in 25 cases 34.2%
Epicanthic fold seen in 17 cases 23.2%
Hernia seen in 7 cases 9.5%

3- Mother and father age

3-1-mother age

Mother age	No. of cases	Percentage
20-25 years	4	5.5
26-30	11	15.1
31-35	16	21.9
36-40	26	35.6
More than 40	16	21.9
Total	73	100

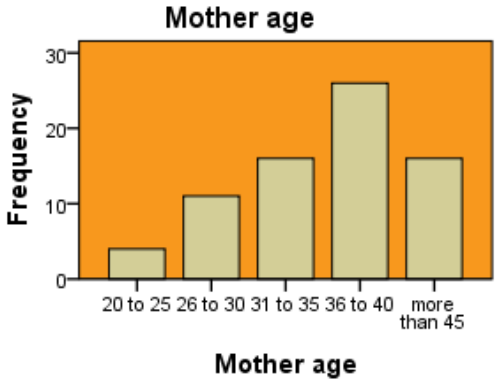

Fig. 1. Histogram showing frequency vs mother age

As we can see in the figure the most risky age group 30 to 40 years.

3-2- father age

Father age	No. of cases	percentages
20-25	1	1.4%
26-30	1	1.4%
31-35	11	15.1%
36-40	17	23.3%
41-45 and more	43	58.9%
Total	73	100%

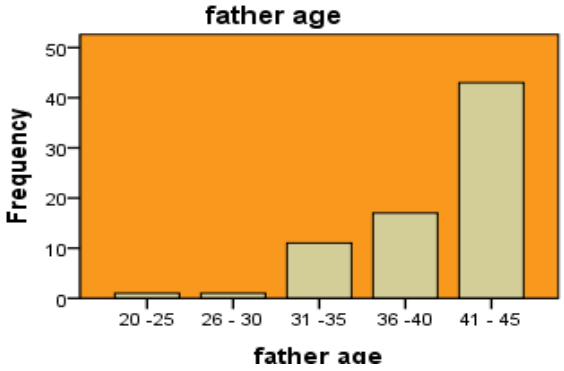

Fig. 2. Histogram showing frequency vs father age

This figure show the risk of having a baby with DS is increasing with an increase father age above 40 years, and this relation to be proved in other study with large number of patient.

Systemic association

1-Congenital heart disease (CHD) by Echocardiography.

We screen all the children, we found 51 cases have congenital heart disease 69.9%, 30 cases of them have Ventriculo- Septal Defect (VSD).

	Number of cases	Percentage
With CHD	51	69.9%
NO CHD	22	30.1%
TOTAL NO.	73	100%

2-Hypothyroidism found in 23 cases 31.5%

	No. of cases	Percentage
Have hypothyroidism	23	31.5%
Don't have	50	68.5%
Total no.	73	100%

3-abdominal ultrasound done for all children the result is as;-

Two cases has nephrocalcinosis, 2.7%.
One case has gallbladder stone 1.36%.
One case has dilated pelvicalyceal system 1.36%

4- GIT abnormalities as:

Hirschsprung disease 3 cases
Duodenal atresia 2 cases

4. DISCUSSION

We compare our study with another one done in India where they study 524 patients over 7.5 years [10].

The result in that study was as follow;-

Craniofacial features noted in 50% of cases.
Upper slanting in 83.9%.
Ear abnormalities 66.9%.
Epicanthic folds in 56.9%.
Flat facial profile 50.9%.
Hypotonia 76.3%.
Sandal sign 46.2%
Simian crease 33.2%.
Cataract 1.9%.
CHD 18.3% and the most common cardiac anomaly was VSD around 25.8% of CHD.

GIT abnormalities as follow;-

Imperforate anus 3 cases, Hirschsprung disease 2 cases, duodenal atresia one case and Morgagni hernia one case.

The cytogenetic abnormalities were available in 42.2%., the nondisjunction is present in 95%, translocation in 3.2% and mosaic in 1.8% [10].

Some features almost have same percentages, and some others defers a lot.

Epicanthic folds is less than the half the other study [10].

The flat facial profile is one of the predominant feature in our study, and is only 50.9% in other study [10].

The CHD is more common in our baby with DS in compare to the other study [10,2].

Endocardial cushion defect also called as atrioventricular cushion defect is most common form which affects up to 40% of the patients. Ventricular septal defect (VSD) is also present in these population which affects up to 35% of the patients [11].

Table 1. When we compare this result with our result we found the comparison as in next table

Feature	Our study	Other study [10]	Other result [2]
Up slanting eyes	98.6%	83.9%	
Epicanthic folds	21.9%	56.9%	
Hypotonia	65.75%	76.3%	
Ear abnormalities	46%	66.9%	
Flat facial profile	95.8%	50.9%	
Sandal sign	79.4%	46.2%	50% [2]
Simian crease	61.6%	33.2%	
Cataract	5.4%	1.9%	
CHD	71.23%	18.3%	40-60% [2]
Hypothyroidism	30%		

Also the GIT anomalies associated with DS is more common in our study;-

Hirschsprung disease in our study is 4.1% and the other study [10] it is 0.38% only.

Duodenal atresia in our study is 2.74%. And in the other study [10] it is only 0.19%.

Gastrointestinal problems in other study [12,13].

DS patients constitute 12% of all cases of Hirschsprung disease (HD).

Duodenal stenosis (DST) and imperforate anus (IA) are 260 and 33 times more likely to occur in DS [12].

HD is a form of low intestinal obstruction caused by the absence of normal myenteric ganglion cells in a segment of the colon [13].

5. CONCLUSION

All features of DS need not to be present in the same individual.

Almost all children diagnosed on clinical examination to have DS, are proved to have nondisjunction type of DS.

Only one case has mosaic DS.

Father age has a big role in DS as a major risk factor, and this should be studied in large number of patients.

The most common features which we found in high percentages are;-

Upper slanting of eyes 98%.
Depressed nose 95%.
Hypotonia 80%.
CHD 71%.

With major deference from other study in some features, and minor differences in others.

CONSENT

As per international standard or university standard, patients' written consent has been collected and preserved by the author(s).

ETHICAL APPROVAL

As per international standard or university standard ethical approval has been collected and preserved by the authors.

COMPETING INTERESTS

Authors have declared that no competing interests exist.

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