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Congenital Anomalies in Down Syndrome Among Qatari Population

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دراسة العيوب الخلقية المصاحبة لمتلازمة داوون في دولة قطر

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تعتبر متلازمة داوون من أهم أسباب التخلف العقلي وعيوب القلب الخلقية. وتؤثر تلك المتلازمة على **300000** فرد وعائلاتهم في الولايات المتحدة الأمريكية فقط. وقد أجرى هذا البحث في الفترة من **2000/1/15** الي **2003/8/7** لدراسة أكثر العيوب الخلقية شيوعا المصاحبة للمتلازمة في الأطفال المصابين بدولة قطر.

وبعد تحليل بيانات **84** حالة تم تشخيصها بمتلازمة داوون وجد أن **55.7** % من الأطفال مصابين بعيب خلقي واحد وأن **19.23** % مصابين بأكثر من عيب خلقي في القلب. بالأضافة الى ذلك وجد أن **46.15** %من الأطفال مصابين بنقص افراز الغدة الدرقية وان **21.79** مصابين بعيوب خلقية في الجهاز الهضمي. وان **6** % من الأطفال قد توفوا قبل بلوغهم ثمانية أشهر من العمر.

Key words: *Down Syndrome, Congenital anomaly, Qatar*

ABSTRACT

Down Syndrome (DS) is the major cause of mental retardation and congenital heart disease affecting the welfare of over 300,000 individuals and their families in USA. The aim of the study is to see which are the most common congenital anomalies associates with Down syndrome in Qatar. Retrospective study performed at Hamad Medical Corporation in Qatar. Data collected from files in the Medical Records over a three and half years from 15/1/2000 to 7/8/2003. Eighty- four cases where all the cases according to a list of trisomy 21 babies taken from the Cytogenetics lab. By reviewing the congenital anomalies associated with Down Syndrome in all these cases, statistical analysis showed high incidence of Down Syndrome 55.7% of the babies in this study had at least one of the heart defects and 19.23 % showed a combination of two cardiac anomalies. In addition, Hypothyroidism was the most common type of both endocrine 46.15 % and thyroid problems and a little proportion of the gastrointestinal tract abnormalities 21.79 % had been reported. Six percent of Down Syndrome babies died in less than 8 months of life.

Introduction

Down Syndrome is a chromosomal defect resulting in characteristic features including a flattened face, thick tongue with extra fissures, extra eyelid folds, lax joints, congenital anomalies of the heart, and mental retardation. Individuals with Down Syndrome have intellectual deficits that occur across a relatively broad spectrum, from an IQ of 20 or below,

to IQ's above 60. Some Down Syndrome individuals are able to achieve semi-independence, while others are profoundly handicapped and remain entirely dependent on care from others [1].

Down Syndrome (DS) is the major cause of mental retardation and congenital heart disease affecting the welfare of over 300,000 individuals and their families in the USA alone [2].In addition, Down syndrome is associated with characteristic set of facial and other physical features, congenital gut disease, and increase risk of leukemia, defects of the immune system, endocrine abnormalities and an Alzheimer-like dementia [3].

People with Down syndrome are subject to a variety of medical conditions. Heart abnormalities that may require surgery are present in about half of all Down syndrome cases. Thyroid problems (underproduction or overproduction of thyroid hormones) affect 10 to 20 percent of people with Down syndrome, but these problems respond well to treatment. The risk of acute leukemia is somewhat increased, although treatment is successful in the majority of cases [4].

There have been dramatic increases in the survival rates of people with Down syndrome since the 1970s. As the risks of medical problems specific to Down syndrome have become known, doctors are now able to recognize those problems earlier, and develop more effective treatments. Today, 44 percent of people with Down syndrome survive to age 60, and this life expectancy is slowly approaching that of people without Down syndrome [5].The present study represents a retrospective study of the major anomalies and age relation associated with a group of 84 cases of DS found in Qatar during the period between 15/1/2000 to 7/8/2003.

Materials and Methods

Hamad Women Hospital is the only governmental hospital in the country. It is also the only place were deliveries occurred. This study, included analysis of the data obtained from 84 women who had given birth to Down Syndrome babies over the last three and half years. The cases were chosen according to a list of all trisomy 21 babies that were diagnosed at the Cytogenetics lab.Data were collected from the patient medical records for variety of variables, including prenatal outcome information such as sex, weight, weeks of delivery, mode of delivery, Apagar score and admission of Neonatal Intensive Care Unit (NICU). Additionally, prenatal investigations as ultrasound, amniocenteses, AFP and chromosomal study, postnatal investigations including chromosomal study, complete blood count (CBC) and list of the congenital anomalies in the baby were also studied. Most of the cases were diagnosed as having Down Syndrome features after birth. A blood sample was analyzed at the Cytogenetics laboratory to confirm the presence of trisomy 21. The babies were then examined for the appearance of the most serious congenital anomalies, such as the congenital heart defects, and then followed up by various pediatric medical groups for the diagnosis of other anomalies and were provided with appropriate assistance. Statistical analysis were done using Mini tab version 12 and SPSS version10 programs as mean, standard error, 95% confidence interval ,and P-value were calculated.

Results

Many risk factors can be related to conception with a Down Syndrome, but the most important one is the advanced maternal age. The ages of the mothers in this study were between 19 and 50 years with a mean of 35.5 ± 65. It was found that the incidence of Down syndrome was significantly related ($P<0.05$) with increased maternal age as shown in Fig 1.

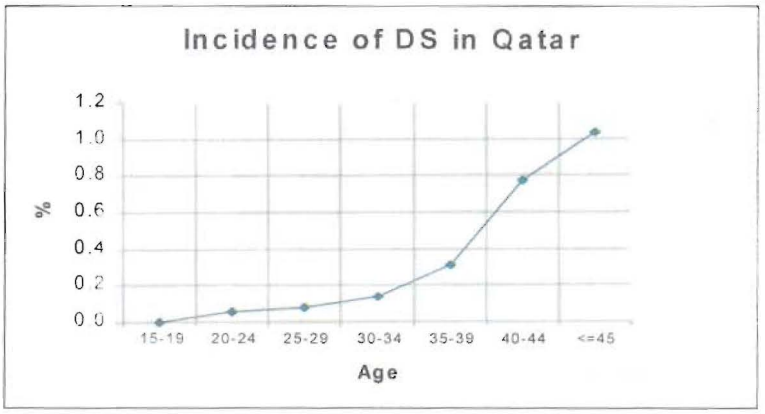

Figure 1 The relation between increased maternal age and risk of Down Syndrome among different age groups

The overall incidence of Down Syndrome in relation to the number of registered live births over the last 3.5 years was nearly the same among non-Qatari females (1.72 per 1000) and Qatari females (1.73 per 1000). It was noticed that the incidence was slightly higher among non Qatari women before the age of 30. While significant higher incidence ($P<0.05$) were found in Qatari for age above 45 years (28%) and almost the same incidence for both groups for ages between 30 to 45 (Fig 2).

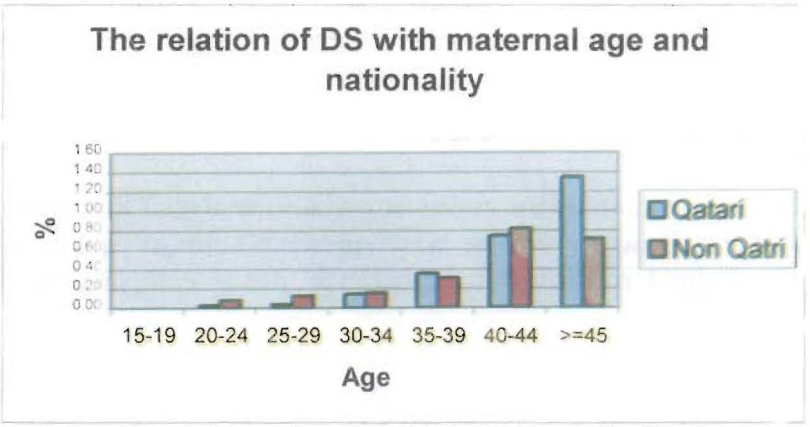

Fig 2. The relation between the nationality of the mother and maternal age

In spite the maternal serum alpha fetoprotein is important for prospecting of the outcome of pregnancy, only data from seven cases were recorded in the files. These results considered inconclusive. The data from cytogenic lab indicated that all the cases had trisomy of 21 karyotype.It is very important to perform Ultrasound investigation during pregnancy to know if there were any abnormalities in the fetus. The investigations of ultrasound were seen in table 1. The results indicated that the estimated fetal weight was in correspondence with the age. In addition, ultrasound diagnosed 7.69% of kidney abnormalities in those fetuses before birth.

Table 1 Ultrasound investigation

Ultrasound Investigations	The variables
Weeks of Ultrasound (wk)	33.3 ± 5.33
Estimated fetal weight (gm)	2338 ± 849
Abnormality seen by Ultrasound: Kidney Brain abnormality Intrauterine growth retardation Heart abnormality	 7.69% 3.08% 3.08% 1.54%
Data presented as mean ± standard error or percentage	

The amniotic fluid is very important for the fetal movement. The study indicated that the percentage of Polyhydramnios was significantly higher in 3rd trimester (table 2).

Table 2 The Ultrasound investigations for the amount of Amniotic fluid in the 2nd and 3rd trimesters

Interval	Normal	Polyhydramnios	Oligohydramnios
2nd trimester	89.23%	10.77%	0%
3rd trimester	54.41%	33.29 %*	12.30%

*** Significant relationship (p-value<0.05).**

The baseline information of the newborn was also analyzed for all study groups. This information showed that Down Syndrome was represented almost equally in both sexes. In addition, there was a slight increases in the preterm infants compared with the premature ones.

It was also obvious that the proportion of under weight between infants was higher than over weight, whereas over half of the deliveries were through normal vaginal delivery and a lesser percentage were cesarean section.

The majority of newborns with Down Syndrome were having an excellent Apgar score (form 7 to 10) and about one fourth of them were admitted to Neonatal Intensive Care Unit (NICU) (table 3).

Table 3The baby outcome

	Descriptive variable	The value
Mode of delivery	Normal vaginal delivery Cesarean section	58.45% 41.56%
Sex	Males Females	48.84% 51.16%
Gestational age	Premature Preterm Term	15.79% 34.21% 50%
Weight	Under weight Ideal weight Over weight	32% 62.67% 5.33%
Apgar score	Excellent Good Bad Unknown	89.19% 6.76% 2.7% 1.35%
	Admission to NICU	27.4%
Data presented as mean ± standard error or percentage		

Down Syndrome is usually associated with multiple congenital anomalies. Figure 3 shows the hematological disorders detected in the groups studied. Thrombocytopenia had the highest significant frequencye (30%) ($P<0.05$) while 10% of the cases had anemia and another 10% had leukocytosis. On the other hand almost half of the group studied showed no indication of any type of hematological disorders.

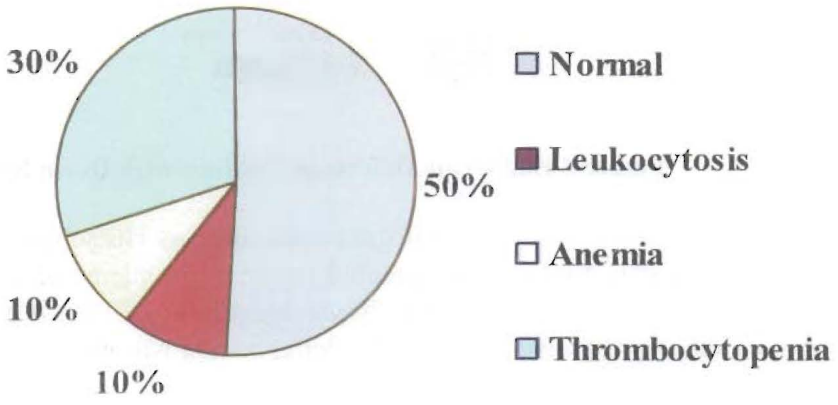

Figure 3 Hematological disorders associated with Down Syndrome

Heart anomaly is considered as one of the most common and dangerous anomalies in Down Syndrome. In this study 55.7% of the cases had been reported to have one or more types of the congenital heart diseases ($P<0.05$). Figure 4 shows the percentage of some of the most common heart defects in this study. The highest incidence found to be the presence of combination of two anomalies (19.23%) as Atrioventricular Canal Defect

(AVD) and Atrial Septal Defect (ASD), Atrial Septal Defect (ASD) and Patent Ductus Arteriosus (DA), and Ventricular Septal Defect (VSD) and Atrial Septal Defect (ASD), where non of the cases showed Atrioventricular Canal Defect alone (0%).

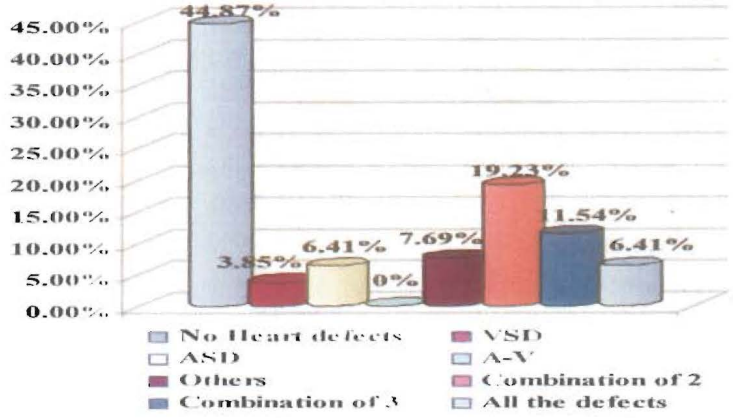

Figure 4 Heart Defects in Down Syndrome

Down Syndrome usually associated with many endocrine dysfunctions, Figure 5 showed that hypothyroidism (46.15%) is significantly an endocrine abnormality in the group studied ($P<0.05$). Whereas; the low level of growth hormone alone or with hypothyroidism were the least common.

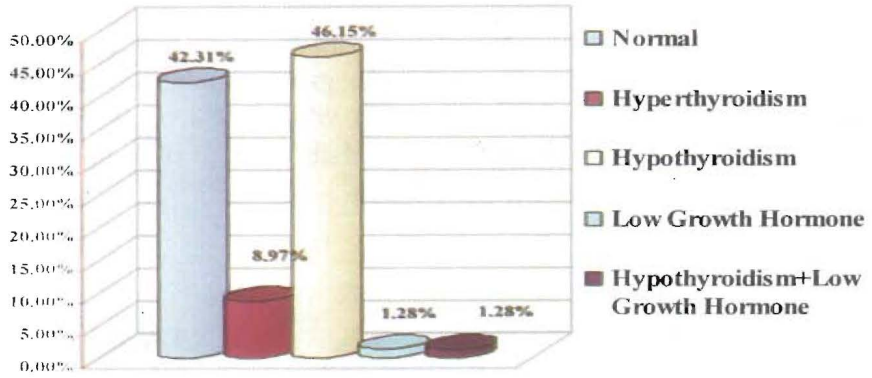

Figure 5 Endocrine Defects in children with Down Syndrome

There were many gastrointestinal tract anomalies as Hurschsprung disease, duodenal atresia and hepatomegaly that can be detected in the early stages of infant's life. The most common anomaly found in this study was hepatomegaly (14.29%). A very low incidence of other anomalies such as Hirschsprung and duodenal atresia was also noticed (Figure 6).

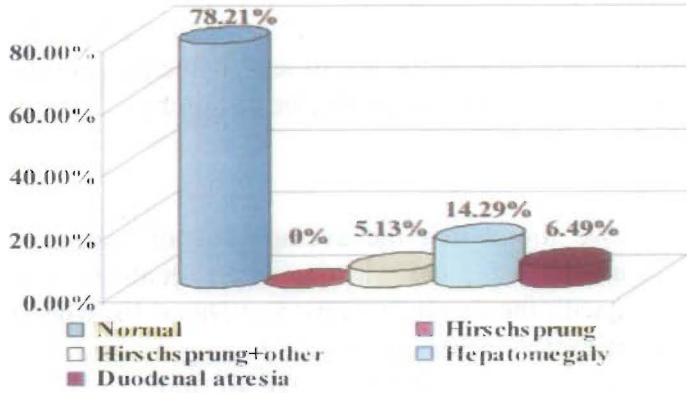

Figure 6 Gastrointestinal Tract defects in Down Syndrome

Many infants with Down Syndrome complained from respiratory tract problems. The results showed that 15.58% of Down Syndrome studied were having anatomical abnormalities in their respiratory tract as enlarged tonsils or adenoids that may lead to obstructive sleep apnea (figure 7).

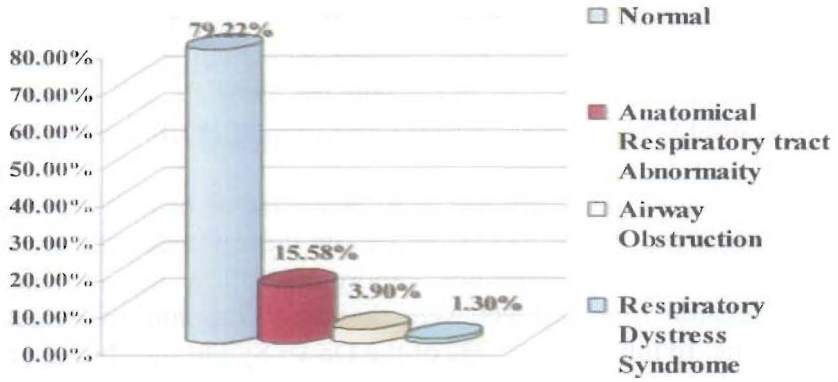

Figure 7 Respiratory Tract Abnormalities in Down Syndrome

Other congenital anomalies found in Down Syndrome children are shown in Figure 8. these anomalies include vision abnormalities as complete loss of vision in one or both eyes or congenital nystagmus, hearing abnormalities as loss of hearing and other orthopedic deformities like chest deformity and costal retraction).

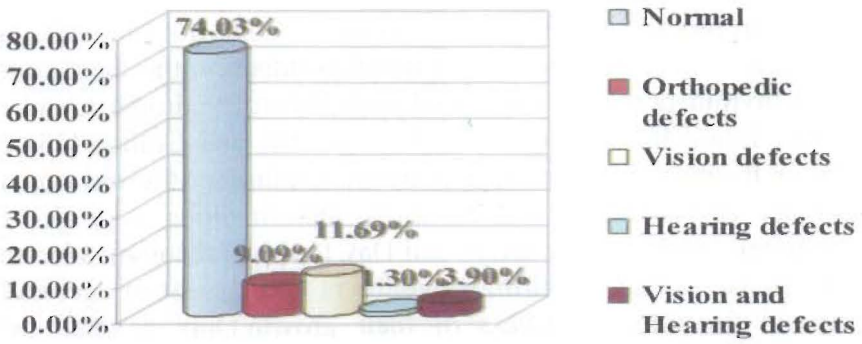

Figure 8 Other Congenital anomalies in Down Syndrome

All the Down syndrome cases studied are surviving by the time that the study was carried on except of 6% that were died at the age of less than eight month, due to Atrioventricular Canal Defects, Septic shock and congestive heart failure.

Discussion

In this study, we found that the average age of women having birth to a Down Syndrome child was about 35.5 ± 6.5 with increased incidence between 33-39 years of age (38.36%). This agreed with the result of Terry and David [6] who stated that women age 35 and older had a significantly increased risk of having a child with Down Syndrome. The incidence increases gradually to one in 100 by age 40, and 1 to 30 at age of 45.

The incidence for DS among the population of Qatar was calculated to be 1 in every 577 with no significant difference between Qatari mothers 1.73/1000 and non Qatari 1.72/1000. This was in agreement with Mark [7] study, who stated that Down Syndrome affects all races and economic levels equally. This incidence is higher than world wide estimate rat of 1/800 [8]. The Heterogenous nature of Qatari population were most of non Qatari are non parent resident and the absence of prenatal diagnosis of genetic counseling could be factor shows this elevation.When Qatari mother were compared to non-Qatari the incidence in relation to different age group was different. The higher incidence was observed among young non-Qatari mothers because most of non Qatari females are among this group which marks the wives of labor forces in the country. Only limited mothers of old age were non Qatari women are living in Qatar therefore Qatari mother showed higher ratio in age over 40.

The results showed that there was high incidence of babies with high level of white blood cells (WBCs) (10%). Robison [9] from Britain indicated that the incidence of leukemia is 1 out of every 100 Down Syndrome children a follow up of these cases is highly recommended.Congenital heart defects were the most common anomalies seen associated with Down Syndrome. In this study 55.7% of the Down Syndrome children had at least one of the heart defects. This is slightly higher than the result of Allan [10] who indicated that 45% of babies with Down Syndrome were born with heart defects. The most common type of heart defects detected was Atrial Septal Defect and the least one was Atrioventricular Septal Defect as it was never found alone. This result is in contrast to which was obtained by Stoll et al., [11]. They found that the commonest defect was Atrioventricular Septal Defect and the least one was Atrial Septal Defect.There was a slight relation between the maternal age and the presence of heart defects in Down Syndrome baby. It was found that about 40% of DS children who had heart defects were born to mothers who were 31-40 years old. In the European study by Stoll [11] 58.7% of live born with Down Syndrome who had congenital heart defects were from mothers under 35 years of age, 21.3% from mothers aged 36 or 37 years and 20% mothers over 37 years of age.Hypothyroidism is the most common type of both endocrine and thyroid problems associated with Down Syndrome found in this study. Simillar results were found by Pozzan et al., [12]. Sharav and Collins [13] explained the cause to be a delay in the maturation of the hypothalamic-pituitary-thyroid axis. In addition, a very small percentage of Human Growth Hormone abnormalities were also due to slight hypothalamic or pituitary problems. Loundon and Day [14] had recommended that all infants with Down Syndrome be checked at birth, 6 months of age, 1 year of age, and once a year thereafter for thyroid function, regardless of their growth.Only a small percent of the gastrointestinal tract abnormalities had been reported in this study. Hirschsprung disease had been reported more frequent in combination with other gastrointestinal tract abnormalities that included gastroeosophygeal reflux, duodenal atresia, hepatomegaly and Megacolon.

According to Zachor [15] gastrointestinal anomalies were frequently associated with Down's Syndrome (12%) and the more common type were duodenal atresia, annular pancreas and Hirschsprung disease. Buchin and Levy [16] has reported that two percent to five percent of children had duodenal atresia. Another 2 percent had Hirschsprung disease. Children with Down Syndrome do have an increased risk of having Hirschsprung disease, and sometimes it could be very difficult to distinguish the difference between Hirschsprung and the normal stooling pattern of a baby with Down Syndrome [17].

Respiratory defects have also reported among the group studied such as lung abnormalities, as fibrosis, Respiratory Distress Syndrome (RDS), pulmonary obstruction and isolated elevated blood pressure in the lungs (pulmonary hypertension) in patients with Down Syndrome. The pulmonary hypertension could be related to malformation of the lung tissue, although the exact cause is not known [18]. Children with Down Syndrome were at risk for respiratory infections. Some respiratory infections are caused by a weak cough, which is sometimes seen in children with hypotonia. Other causes of respiratory infection are heart problems leading to fluid in the lungs, regurgitation of food from the stomach into the lungs, and weakened immune systems [19].

Several other defects that associated with Down Syndrome children were also noticed in this study, but had been represented in very low frequency. These abnormalities included orthopedic defects as costal retraction and chest deformity, Vision abnormality as Congenital Nystagmus, loss of vision as eye abnormalities, and finally Hearing abnormalities as ear defects and loss of hearing. Children with Down Syndrome experience a wide range of orthopedic problems due to their loose ligaments and hypotonia [20]. In addition, Balkany et al., [21] reported that the incidence of hearing loss in Down Syndrome was between 38-78%

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