Incidence and outcome of renal anomalies in children with down syndrome
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ABSTRACT

Background
Down syndrome is one of the most common occurring chromosomal disorders, which involves multiple systems. Renal and urinary tract anomalies have been reported to occur at increased frequency among this population.

Aims
This study aims to estimate the prevalence of renal anomalies in Down syndrome patients, as well as to evaluate their outcome.

Methods
A retrospective study was conducted in the tertiary hospital, KAUH, from the period of August to October 2016. Files and medical records of 261 patients diagnosed with Down syndrome were reviewed and retrieved from the years 2005–2016.

Results
Out of the 241 patients, 113 (46.9 per cent) were screened by ultrasound imaging. Renal abnormalities were detected in 51 (21.2 per cent) patients. Of whom 20 (39.2 per cent) were females and 31 (60.8 per cent) males. Abnormalities detected on imaging consisted of: hydronephrosis, vesicoureteral reflux, obstruction, malpositioned kidney, renovascular anomalies and others.

The outcomes of the patients with renal involvement were as following: five patients (9.8 per cent) developed chronic kidney disease, eight (15.7 per cent) died due to different causes: (DIC, multiple organ failure, Respiratory arrest, sepsis, and unspecified), and 38 (74.5 per cent) showed no progression of the renal disease.

Conclusion
The prevalence of renal abnormalities in Down syndrome was found to be high so early screening for Down syndrome patients is recommended to help diagnose them earlier. Further studies are recommended to follow up Down syndrome patients with renal abnormalities.

Key Words
Down syndrome, renal anomalies, hydronephrosis

What this study adds:
1. What is known about this subject?
Renal anomalies in DS are considerably higher than in non-DS population, with the risk being 3.5 times more among liveborn infants with DS. Another study also stated that the prevalence was higher, being 3.2 per cent in DS population compared to 0.7 per cent among non-DS, which means four to five times greater than in the public population.

2. What new information is offered in this study?
We found a high incidence of renal anomalies in children with Down syndrome.

3. What are the implications for research, policy, or practice?
Because of the high incidence of renal anomalies in Down syndrome, we believe that routine screening for renal anomalies is important so that early therapeutics and intervention measurements can be done in a time appropriate.
Background

Down syndrome also known as trisomy 21, is one of the most common occurring chromosomal disorders, with an incidence of one in 554 live births (1.8 per 1,000) in the Saudi Arabian population. Worldwide, the incidence is estimated to be one in 1,000 live births, according to the WHO. Down syndrome Children have multiple malformations, medical conditions, and cognitive impairment because of the presence of extra genetic material from chromosome 21.

Down syndrome is associated with congenital anomalies in different organ systems, the most common in descending order, are: cardiac, digestive, musculoskeletal, renal then respiratory. Thus, there are guidelines to screen Down syndrome children for those possible associations, via extensive history and physical examination as well as imaging and other modalities as needed. At birth to one month of age all Down syndrome children are screened by an Echocardiogram, as well as hearing assessment, and thyroid-stimulating hormone (TSH) for congenital hypothyroidism. These are examples of some of the guidelines from the American academy of paediatrics being followed regarding down syndrome patients in the neonatal period.

Renal and urinary tract anomalies have been reported to occur at increased frequency among persons with Down syndrome with a wide ranging incidence estimated from 3.5–21.4 per cent in different studies. With the increased incidence it is reasonable to be concerned about the outcome of such patients.

Regardless of those reports, routine renal and urological screening is not yet recommended nor a standard of care in most parts of the world, due to scarce studies in the literature to confirm this increase in prevalence. Up to our knowledge, renal anomalies in regard to Down syndrome have not been discussed before in Saudi Arabia and in particularly Jeddah. This study aims to add to the literature by estimating the prevalence of renal anomalies in patients with Down syndrome in King Abdulaziz University Hospital, as well as to evaluate their outcome.

Method

This is a retrospective descriptive study conducted in King Abdulaziz University Hospital (KAUH), Jeddah, Saudi Arabia. From the period of August to October 2016. Approval for the study was permitted by the ministry of higher education, King Abdulaziz University, Ethics committee. Files and medical records of patients diagnosed with Down syndrome were reviewed. All Down syndrome patients of different age groups being followed up at KAUH, who had accessible and complete data files, were included in the study. Therefore, patients with incomplete files were excluded.

The data obtained comprised of essential demographics such as age, gender and nationality. In addition, the following were considered: any diagnosed congenital anomaly (cardiovascular, respiratory, gastroenterology, renal, haematology, musculoskeletal, endocrine, ophthalmology and neurology), any complaints of urinary symptoms recorded in the files (dysuria, recurrent UTI, enuresis, voiding dysfunction, incontinence, change in urine colour, haematuria) and if the patient had hypertension. Also, any radiological imaging data (renal ultrasound, abdominal X-ray, DMSA scan, MCUG and DTPA) was obtained.

Details about the outcome of the patients were considered, such as the progression to chronic kidney disease (CKD) which is described as damage to the kidney or a glomerular filtration rate of less than 60mL/min/1.73m² for as long as three or more months, regardless of the cause. Lastly, the need for dialysis or the death of the patient was also obtained.

Patients throughout the study were considered to have renal involvement if either a previous diagnosis of renal anomaly was documented in the patient’s file based on thorough history, physical examination and investigations or if any abnormal renal findings were discovered on radiological imaging. Only those with congenital anomalies or a history of anomalies were included in our study as renal involvement, discarding any acquired renal conditions.

Data were statistically analysed by SPSS version 16 using descriptive statistics as frequencies. The results were compared to the studies in the literature.

Results

A total of 261 data was collected; twenty patients were excluded from the study due to missing data. We included 241. Down syndrome patients between the ages of one month to 57 years (median nine years). Among them 139 (57.7 per cent) male and 102 (42.3 per cent) female (Table 1).

The most commonly associated system involvement was the cardiac system, which was affected in 137 (56.8 per
cent) of the patients. Other systems involved are as shown in Figure 1.

Out of the 241 patients, renal abnormalities were detected in 51 (21.2 per cent) patients as Figure 2 shows. Of whom 20 (39.2 per cent) were females and 31 (60.8 per cent) males. Radiological imaging detected renal abnormalities in 35 (68.6 per cent) patients, while 16 (31.4 per cent) were already found to have had a previous documented diagnosis.

Renal ultrasound was performed for 49 (98.1 per cent), DMSA scan for five (9.8 per cent), Micturating cystourethrogram (MCUG) for nine (17.6 per cent), DTPA scan for eight (15.7 per cent) and x-ray KUB for 12 (23.5 per cent). Abnormalities detected on imaging consisted of: hydronephrosis, vesicoureteral reflux, obstruction, malpositioned kidney, Renovascular anomalies and others. Figure 3 shows further details.

The outcome of the patients with renal involvement was the following: five patients (9.8 per cent) developed chronic kidney disease, eight (15.7 per cent) died due to different causes: (DIC, multiple organ failure, Respiratory arrest, sepsis, and unspecified), and 38 (74.5 per cent) showed no progression of the renal disease.

Discussion

The prevalence of renal and urinary tract anomalies among Down syndrome found in our study is 21 per cent. A much lower number was found by Jaun C, estimated as 3.2 per cent. Other studies provided early estimates of the incidence varying widely from 3.2–21.4 per cent. In which some included autopsy cases of Down syndrome, while some had the limitation of a small sample size. The prevalence is considerably higher than in non-Down syndrome population, with the risk being 3.5 times more common among live-born infants with Down syndrome. Another study stating the higher prevalence of 3.2 per cent in Down syndrome population compared to 0.7 per cent among non-Down syndrome, which is four to five times greater than in the public population. Our study confirms the increased prevalence of renal anomalies among Down syndrome children as found in the previously mentioned studies.

Furthermore, we found the following abnormalities, from the most common to the least common: Isolated hydronephrosis (35.5 per cent), vesicoureteral reflux, obstruction, malpositioned kidney, renovascular anomalies and others. All of these conditions are associated with possible complications affecting the kidney function if left untreated or undetected. Comparatively in a registry based study done in New York State done on 3,832 down syndrome patients, Juan C. revealed that Children with down syndrome had significantly increased risks of anterior urethral obstruction, cystic dysplastic kidney, hydronephrosis, hydroureter, hypospadias, posterior urethral valves (PUV), prune belly syndrome, and renal agenesis.

In this study we focused on congenital renal anomalies and did not include glomerular diseases. Although interestingly, Said et al. reviewed the clinical-pathologic characteristic of 17 patients with Down syndrome who underwent renal biopsy and found IgA nephropathy (n=5) and focal segmental glomerulosclerosis (n=4) being the most common glomerular diseases in his cohort.

It has also been found that children with congenital hypothyroidism have an increased prevalence of congenital renal and urologic anomalies. The authors of the study suggested ultrasound screening for those children. Down syndrome patients may also present with primary glomerulonephritis if they have an autoimmune disease (celiac disease, alopecia or hypothyroidism).

Not many studies discussed the outcome of Down syndrome patients with renal congenital anomalies, chronic kidney disease developed in five (9.8 per cent) of our study, of whom some underwent dialysis. Hence, with the increased risk of renal and urinary anomalies comes an increased morbidity rate, possibly leading to dialysis or transplant and an increase in cost, and use of resources. Although not entirely similar to our study as Said et al. study reviewed the clinical-pathologic characteristic of renal biopsies, it is worth noting that his study presented eight patients who had chronic kidney disease; Six patients progressing to end stage kidney disease, four of whom died.

Our result emphasizes the need for routine ultrasound as an early screening and diagnosis to prevent the progression of renal and urinary tract anomalies. Among our sample less than half of the patients (46.9 per cent) were screened by ultrasound.

Interestingly, in comparison to the other anomalies found among our study the most common associated anomaly was found to be congenital heart diseases (CHD) 137 (56.8 per cent), which is consistent to several studies as well. Following CHD was the respiratory system then the renal
anomalies being the third most common. This is in agreement to Cleves et al. study where genitourinary anomalies were the third most common defect found in Down syndrome, after cardiac and gastrointestinal anomalies. Thus, this concludes that renal anomalies are not rare among Down syndrome patients.\textsuperscript{11}

**Conclusion**

The prevalence of renal abnormalities in Down syndrome was found to be high so early screening for Down syndrome patients is recommended to help diagnose them earlier. Further studies are recommended to follow up Down syndrome patients with renal abnormalities.

**References**


**PEER REVIEW**

Not commissioned. Externally peer reviewed.

**CONFLICTS OF INTEREST**

The authors declare that they have no competing interests.

**FUNDING**

None

**ETHICS COMMITTEE APPROVAL**

Ethical committee at King Abulaziz University. Reference 256677.

**Table 1: Demographic data of DS patients with and without renal involvement**

<table>
<thead>
<tr>
<th></th>
<th>DS without renal involvement</th>
<th>DS with renal involvement</th>
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<tbody>
<tr>
<td><strong>Median Age</strong></td>
<td>9 years</td>
<td>7 years</td>
</tr>
<tr>
<td><strong>(Range)</strong></td>
<td>(1m–57yr)</td>
<td>(2m–38yr)</td>
</tr>
<tr>
<td><strong>Gender, n (%)</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td><strong>Female</strong></td>
<td>102 (42.3%)</td>
<td>20 (39.2%)</td>
</tr>
<tr>
<td><strong>Male</strong></td>
<td>139 (57.7%)</td>
<td>31 (60.8%)</td>
</tr>
</tbody>
</table>
Figure 1: Associated anomalies with Down syndrome

Figure 2: Renal involvement in Down syndrome

Figure 3: Renal abnormalities detected by radiographic tests