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EC MICROBIOLOGY
Research Article

Medical Complication of Down Syndrome: Systematic Literature Review

Nouf Abdulhadi Al Alhadi[1]*, Murtadha Ahmed Alatawi[2], Hassan Abdulaziz Alali[3], Hamad Ayedh Almarri[4], Khaled Waleed Alenezi[4], Zohoor Muteb Almalki[5], Wejdan Abdullah Alyamani[6], Abdulmohsen Mohammed AlShehri[7], Rayan Abdulrhman Alasmari[7] and Abdulaziz Hassan Alqarni[7]

[1]Jazan University, Jazan, Saudi Arabia

[2]Abdulrahman Bin Faisal University, Dammam, Saudi Arabia

[3]King Faisal University, Al-Ahsa, Saudi Arabia

[4]Adan Hospital, Kuwait, Kuwait

[5]King Fahad Hospital, Albaha, Saudi Arabia

[6]Batterjee Medical College, Jeddah, Saudi Arabia

[7]King Khalid University, Abha, Saudi Arabia

***Corresponding Author:** Nouf Abdulhadi Al Alhadi, Jazan University, Jazan, Saudi Arabia.

Received: November 01, 2020; **Published:** November 28, 2020

Abstract

This review is aiming to discuss and provide high level, clinically relevant, information on the medical complications related to DS and its prevalence among the patients. the presented review was conducted by searching in Medline, Embase, Web of Science, Science Direct, BMJ journal and Google Scholar for, researches, review articles and reports, published over the past years. Were searched up to November 2020 for published and unpublished studies and without language restrictions, if several studies had similar findings, we randomly selected one or two to avoid repetitive results. Based on the findings and results of this review, Prevalence of the medical complication among patients with DS is depend on many age of the patient. socioeconomic status, primary health care, early detection and the advances of the management approaches. Many complications can occur to patient with DS and they all related to increase in the production of specific protein which affect the cardiovascular system (CVS) and there's higher incidence of Patent ductus arteriosus compared to the other CVS disorders, in addition to higher incidence of thyroid and bones problems and overweight in patients with DS when compared to the general population.

Keywords: *Complications; Down Syndrome; Trisomy 21; Intellectual Disability; Health Comorbidities; Prevalence; Genetic*

Abbreviations

DS: Down Syndrome; CHD: Congenital Heart Diseases; AD: Alzheimer's Diseases; HD: Hirschsprung Disease; BMD: Bone Mineral Density; HOMA: Homeostasis Model Assessment; CVS: Cardiovascular System

Introduction

Down syndrome (DS) is considered to be the most common diagnosed genetic in united states and UK [1] and the most common leading cause of intellectual disability which affect millions of patients worldwide those problem take several forms for example learning and memory, congenital heart diseases (CHD), Alzheimer's diseases (AD), leukemia, cancers and Hirschsprung disease (HD). There's three

types of down syndrome but the most common one is Trisomy 21 affect more than 95% of the patient and the others types include Translocation Down syndrome and Mosaic Down syndrome [2].

Co-morbid disease and medical complications is commonly occurring with DS and all most affecting all of the body organs as result of increase in the production of specific proteins [3]. Patients with DS have significant physical feature that mark them like the low set ears, up-slanting palpebral fissures, flat nasal bridge, and a single palmar crease [4]. During the recent days and as result of enhanced medical care and the early dedication and the treatment of the complication the life expectancy of the patient with DS is increased from 10 years in 1940 to more than 47 in 2013 [5]. We are aiming through this systemic review to provide high level, clinically relevant, information on the medical complication related to DS and its prevalence among the patients.

Materials and Methods

The present review was conducted in November 2020 under the preferred reporting items for systematic reviews and meta-analyses (PRISMA) declaration standards for systematic reviews. We reviewed all the topics related to medical complications of DS and its prevalence among the patients.

Our search was completed without language restrictions. Then we extracted data on study year, study design, and key outcome on medical complications of DS.

The selected studies were summarized and unreproducible studies were excluded. Selected data are shown in table 2.

Studies have been rated as being high quality by an established evaluation process based on the DyunaMed criteria and it's based on the level of evidence as follows:

- **Level 1 (likely reliable) evidence:** Representing research results addressing clinical outcomes and meeting an extensive set of quality criteria that minimize bias. Example: Randomized controlled trial/meta-analysis.
- **Level 2 (mid-level) evidence:** Representing results addressing clinical outcomes, and using some methods of scientific investigation but not meeting the quality criteria to achieve level 1 evidence labeling. Example: well-designed non-randomized clinical trials.
- **Level 3 (lacking direct) evidence:** Representing reports that are not based on scientific analysis of clinical outcomes. Examples include case series, case reports, expert opinion, and conclusions extrapolated indirectly from scientific studies.

Inclusion criteria

Inclusion criteria were: Current methods of, medical complications of DS.

Exclusion criteria

Irrelevant articles [not related to the aim of this review and articles that did not meet the inclusion criteria in this review.

Data extraction and analysis

Information relating to each of the systematic review question elements was extracted from the studies and collated in qualitative tables. Direct analysis of the studies of the medical complications of DS.

Results and Discussion

There's many medical complications from DS all most affecting all of the body organs, so for the purpose of the report we have listed the complication and its subtypes in a thematic analysis methodology in table 1 [6].

Congenital heart disease 9[a] (14)
Septal defect
Patent ductus arteriosus
Tetralogy of Fallot
Congenital valvular disease
Endocrine disorders
Hypothyroidism
Coeliac disease
Type 1 diabetes mellitus
Seizures
Adult onset
Child onset
Psychiatric Disorders
Depression
Alzheimer's disease
Hearing deficit
Eczema 15 (23)
Osteoarthritis 9 (14)

Table 1: *List of the medical complications of DS.*

Cardiac disease

A Hospital Based Review of Cases conducted in Tikur Anbessa Specialized Hospital, in Ethiopia, 116 patients with DS know to have cardiac anomalies (53 males and 63 females) between April 2010 and May 2015 were made. "Patent ductus arteriosus occurs in 57 (36.5%), Ventricular septal defect in 31 (19.9%), Atrial septal defect in 30 (19%), Atrio-ventricular septal defect in 29 (18.6%), Tetralogy of Fallot in 4 (2.6%) and others in 5 (3.2%) cases. Cases were alive, lost to follow-up and died in 59, 35 and 22 cases, respectively" [7].

Endocrine disorders

endocrine disorders are highly prevalent in patients with DS, including musculoskeletal; as study conducted in University Hospital Marqués deValdecilla and the Down Syndrome Foundation of Cantabria (Spain), 151 males and female (75 have DS and 76 controls) all are above the 18 years old. "DS individuals had lower height (151 ± 11 vs. 169 ± 9 cm). BMD was higher in the controls (lumbar spine (LS) 0.903 ± 0.124 g/cm^2 **in patients and 0.997 ± 0.115 g/cm^2 in the** controls; femoral neck (FN) 0.761 ± .126 g/cm^2 **and 0.838 ± 0.115 g/cm^2**, respectively). vBMD was similar in the DS group (LS 0.244 ± 0.124 g/cm^3; FN 0.325 ± .0.073 g/cm^3) and the controls (LS 0.255 ± 0.033 g/cm^3; FN 0.309 ± 0.043 g/cm^3)".

Another retrospective cohort study conducted in 159 neonates with Down syndrome, born during the period 1998 - 2007 screening to assess thyroid functions and compared to the general population. "tT4 concentrations in children with Down syndrome were significantly lower, and TSH higher than those in the general population" [9].

Diabetes mellitus

Study to assess the prevalence of insulin resistance among persons with DS show that "Five patients were adults (Tanner V or presence of menarche), 9 pubertal (Tanner II - IV) and 1 prepubertal (Tanner I). No one had AN. Two were obese, 4 overweight and 9 normal. Considering the total number of patients, HOMA was 1.7 ± 1.0, insulin 9.3 ± 4.8 μU/ml and glucose 74.4 ± 14.8 mg/dl. The HOMA values were 2.0 ± 1.0 in females and 1.5 ± 1.0 in males. Considering the nutritional classification, the values of HOMA and insulin were: HOMA: 3.3 ± 0.6, 2.0 ± 1.1 and 1.3 ± 0.6, and insulin: 18.15 ± 1.6 μU/ml, 10.3 ± 3.5 μU/ml and 6.8 ± 2.8 μU/ml, in the obese, overweight and normal groups respectively. Considering puberty, the values of HOMA and insulin were: HOMA: 2.5 ± 1.3, 1.4 ± 0.6 and 0.8 ± 0.0, and insulin: 13.0 ± 5.8 μU/ml, 7.8 ± 2.9 μU/ml and 4.0 ± 0.0 μU/ml, in the adult, pubertal and prepubertal groups respectively" [10].

Overweight

Study was conducted to compare the incidence of overweight among patients with DS compared to the statistics of the general populations, study founded that there is higher incidence of overweight among patient with DS [11].

Author and year	Sample	Complication	Findings
Muntha A. 2019 [7]	116	Cardiac disease	- Patent ductus arteriosus 57 (36.5%) - Ventricular septal defect in 31 (19.9%) - Atrial septal defect in 30 (19%) - Atrio-ventricular septal defect in 29 (18.6%) - Tetralogy of Fallot in 4 (2.6%) - others in 5 (3.2%) cases.
García-Hoyos M, 2016 [8]	75 patients with DS and 76 controls	Reduced Bone mineral density (BMD)	Areal BMD is reduced in DS, but it seems to be related to the smaller body and skeletal size.
Erlichman I, 2016 [9]	159 neonates with Down syndrome	Thyroid disorder.	tT4 concentrations in children with Down syndrome were significantly lower, and TSH higher than those in the general population
Fonseca, C.T. 2005 [10]	15 adolescents with DS (8 males and 7 females) were studied, aged 10 to 18 years	Insulin resistance	The obese and overweight, female and adult patients showed the highest values of Homeostasis Model Assessment (HOMA) and insulin
Rubin SS, 1998 [11]	283 persons with Down syndrome	Overweight	Study found a higher prevalence of overweight in patients with DS compared to the general population.

Discussion

Postoperative the medical complication of the DS is affecting all the body organs and the survival rate is primarily depending on the early detection and the advances of the management approaches, others factors may also affect the outcomes and the survival rate like the socio-economic status and primary health care provided to the patients.

List of complications that can occur to the patients with DS and it's detected in early childhood in the most of the case especially the cardiovascular problems and the endocrine problem and they might be the main source of the problem that affect all of the body organs.

Patent ductus arteriosus shown to be the highest in incidence among the cardiovascular disease that affect patients with down syndrome, in addition to the higher prevalence of endocrine disorder that affect the thyroid and the bone density in patients with DS when they are compared with the general population [6-10].

Conclusion

Prevalence of the medical complication among patients with DS is depend on many age of the patient. socioeconomic status, primary health care, early detection and the advances of the management approaches. Many complications can occur to patient with DS and they all related to increase in the production of specific protein which affect the cardiovascular system (CVS) and there's higher incidence of Patent ductus arteriosus compared to the other CVS disorders, in addition to higher incidence of thyroid and bones problems, and overweight in patients with DS when compared to the general population.

Conflict of Interest

The authors of this article hasn't receive and support for this work and it was completely self-funded.

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Volume 16 Issue 12 December 2020