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Prevalence of Infectious Diseases Among 6078 Individuals With Down Syndrome in the United States

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Abstract

A recent disease prevalence study of the largest documented Down syndrome (DS) cohort in the United States strongly suggested significant disparity in general infectious disease conditions among individuals with DS versus those without DS. In this follow-up retrospective analysis, we explored these differences in greater detail by calculating prevalence of 52 infectious diseases, across 28 years of data among 6078 individuals with DS and 30,326 age- and sex-matched controls, abstracted from electronic medical records within a large Midwestern health system.

We found that the DS cohort had higher prevalence of pneumonias (including aspiration, viral, bacterial, pneumococcal, and unspecified/atypical); otitis externa; and the skin infections impetigo, abscess, and cellulitis. To the contrary, the DS cohort had lower prevalence of many respiratory infections other than pneumonia (including influenza, strep pharyngitis, upper respiratory infection, sinusitis, tonsillitis, laryngitis, bronchitis, scarlet fever, and otitis media); sexually transmitted infections (including bacterial vaginosis, chlamydia, genital herpes, HIV/AIDS, human papillomavirus, pelvic inflammatory disease, and trichomoniasis); mononucleosis; shingles; unspecified hepatitis; intestinal infections; and enteritis. These findings highlight that individuals with DS could be more or less prone to different infectious diseases than their non-DS matched counterparts. Additional research to understand why these differences exist and how they might affect the clinical approach to patients with DS is warranted. (*J Patient Cent Res Rev.* 2022;9:64-69.)

Keywords Down syndrome; prevalence; infectious disease; pneumonia; skin; influenza; sinusitis; bronchitis; STI

A recent study of the largest documented cohort of individuals with Down syndrome (DS) in the United States described the prevalence of a broad range of disease conditions.[1] Findings strongly suggested a particularly significant disparity in infectious disease among individuals with DS when compared with age- and sex-matched individuals without DS.[1]

Individuals with DS may be particularly vulnerable to infectious diseases due to factors that increase risk of contracting infections, including an impaired immune system, an accelerated aging process, and structural abnormalities.[2-6] Reduced T- and B-cell counts, a smaller thymus size, subpar antibody response to vaccinations, and decreased chemotaxis seen in individuals with DS contribute to their decreased immune response.[2] It is well known that pneumonias are widespread in adults with DS, with increased hospitalization and mortality; however, other infectious disease prevalences are less known.[2-9]

While it has been reported that individuals with DS have lower prevalence of sexually transmitted infections (STIs) than the general population;[10] very little research has gone into characterizing STIs in children and adults with DS. In the general population, chlamydia, gonorrhea, and syphilis have been on the rise for the past several years,[11] further warranting an examination into STI rates in the DS population to better guide sex education guidelines. Given that prevalence of DS itself is increasing[4] and that the lifespan for individuals with DS continues to grow,[3-7] diving further into the specific infections unique to this population is critical to best tailor care.

Herein, this study utilized clinical data representing the largest reported sample of individuals with DS in the United States, treated across a single Midwest-based integrated health system that includes the largest

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center of DS care for adolescents and adults, to explore infection prevalences among those diagnosed with DS. Learning critical information on the most common infectious diseases seen in these individuals might serve to better guide practitioners in their attempts to provide patient-centered care.

METHODS

This retrospective, descriptive cohort study, which utilized 28 years of available encounter data (May 1991–September 2019) abstracted from electronic medical records collected from all sites within one of the largest nonprofit health systems in the United States, was determined to be non-human subjects research by the institutional review board. Full details on the data collection methods for this overall study population can be found in the previously published parent report.[1]

Participants

A total of 6078 cases, deemed eligible for inclusion based on having at least 1 encounter with an International Classification of Diseases (ICD) code of DS, were identified. Comparable control patients included up to 5 individuals without a diagnosis of DS who were matched to each case on year of birth (±1 year) and sex by a data analyst. This approach resulted in 30,326 eligible controls. Of the 6078 cases, 64 were assigned only 4 (as opposed to 5) matched controls.

Procedures

This study design preidentified specific infectious disease conditions of interest to assess prevalence among individuals with DS versus those without. Conditions were chosen based on existing literature and the clinical expertise of one of the authors (B.C.). This study used the U.S. Clinical Modification (CM) codes for medical diagnoses based on the statistical classification of disease denoted in the World Health Organization's publication of the ICD.[12] Specifically, 10th Revision (ICD-10-CM) and 9th Revision (ICD-9-CM) codes were used. A few conditions of interest did not align clearly with ICD-9-CM codes and, instead, AHRQ CCS categories were used. See Table 1 for a complete list of infectious disease conditions of interest and associated ICD codes.

Statistical Methods

Demographics are reported as means with standard deviations and medians with ranges for age and total encounters per sample. Sex, race, ethnicity, and insurance type are reported as counts with percentages. Clinical conditions are reported as counts with percentages and odds ratios (OR) representing the odds of cases having an infectious disease relative to controls. Corresponding Pearson's chi-squared P-values represent statistically significant differences (at an alpha of <0.05) in prevalence of diagnoses between cases and controls. Fisher's exact P-value was interpreted when any sample count was less than 5.

RESULTS

The DS case population was predominantly White (77.35%) and of non-Hispanic/Latino ethnicity (73.51%). Cases had a median of 6 total encounters (ie, clinical visits in the health system) in the dataset. The control cohort was also predominantly White (61.97%) and of non-Hispanic/Latino ethnicity (81.72%), with a median of 7 total encounters in the dataset. Both groups were approximately 52% male and had a median age of 25 years. For complete demographics of the DS and matched control cohorts, the reader is referred to the relevant table published within this project's parent article.[1]

The following paragraphs highlight statistically significant ORs (95% CI) and P-values that were derived from comparing prevalence of clinical infectious disease conditions of interest among individuals with DS (ie, cases) to matched controls. Table 2 shows both significant and nonsignificant analysis results.

Relative to controls, individuals with DS had significantly *greater* odds of experiencing any pneumonia (OR: 4.13 [3.74, 4.56]; P<0.0001) and, specifically, aspiration (OR: 10.50 [7.73, 14.28]; P<0.0001), viral (OR: 13.14 [8.12, 21.26]; P<0.0001), bacterial (OR: 4.72 [3.52, 6.33]; P<0.0001), pneumococcal (OR: 6.87 [2.76, 17.09]; P<0.0001), and unspecified or atypical pneumonia (OR: 3.69 [3.31, 4.11]; P<0.0001). The DS cohort also had more frequent otitis externa (OR: 1.68 [1.42, 1.98]; P<0.0001) and one or more of the skin infections impetigo, abscess, and cellulitis (OR: 1.74 [1.62, 1.88]; P<0.0001).

Conversely, relative to controls, individuals with DS had *lesser* odds of experiencing the following infectious diseases: influenza (OR: 0.62 [0.52, 0.75]; P<0.0001); streptococcal pharyngitis (OR: 0.27 [0.22, 0.33]; P<0.0001); upper respiratory infection (OR: 0.37 [0.34,0.40]; P<0.0001); sinusitis (OR: 0.38 [0.34, 0.42]; P<0.0001); tonsillitis (OR: 0.58 [0.51, 0.65]; P<0.0001); laryngitis (OR: 0.81 [0.68, 0.97]; P=0.0218); bronchitis (OR: 0.48 [0.42, 0.56]; P<0.0001); scarlet fever (OR: 0.36 [0.17, 0.78]; P=0.0070); otitis media (OR: 0.77 [0.70, 0.85]; P<0.0001); and the STIs bacterial vaginosis (OR: 0.14 [0.10, 0.19]; P<0.0001), chlamydia (OR: 0.07 [0.01, 0.53]; P<0.0001), genital herpes (OR: 0.08 [0.03, 0.21]; P<0.0001), HIV/AIDS (OR: 0.31 [0.13, 0.77]; P=0.0074), human papillomavirus (OR: 0.35 [0.21, 0.59]; P<0.0001), pelvic inflammatory disease (OR: 0.29 [0.12, 0.72]; P=0.0045), and trichomoniasis (OR: 0.08

Table 1. Infectious Disease Conditions of Interest and Associated Codes

Infection type	ICD-10-CM code	ICD-9-CM or AHRQ[24] code
Respiratory		
Coronaviruses (excludes COVID-19)	B342	07989
Diphtheria	A36	032
Influenza	J09–J11	AHRQ 123
Haemophilus influenzae type B	A492	0415
Measles	B05	055
Mumps	B26	0727–0729
Rubella (German measles)	B06	056
Whooping cough (pertussis)	A37	033
Strep pharyngitis	J020	0340
Upper respiratory infection	J069	4659
Sinusitis	J01, J32	461, 473
Tonsillitis	J03, J35	463, 47400–47402
Laryngitis	J04–J05, J37	4640, 4760
Bronchitis	J20	AHRQ 125, 490, 49122
Scarlet fever	A38	0341
Otitis media	H669	3829
Pneumonia	J12–J15, J18, J690	AHRQ 122
Aspiration	J12–J15, J18, J690	AHRQ 122
Viral	J12	4809
Bacterial	J15	4829
H. influenzae-caused	J14	4822
Pneumococcal	J13	481
Unspecified/Atypical	J18, J690	486, 5070
Sexually transmitted		
Bacterial vaginosis	N76	61610
Chlamydia	A55–A56	07988, 07998
Gonorrhea	A54	098
Genital herpes	A60	0541
HIV/AIDS	B20	AHRQ 5
Human papillomavirus	R8781–R8782	0794
Pelvic inflammatory disease	A1817, A5424, A5611, N73, N74	614
Syphilis	A50–A53	090–097
Trichomoniasis	A59	131
Urinary tract infection	N398	5990
Other infection		
Otitis externa	H609	38010
Infectious mononucleosis	B27	075
Zika	A925	0663
Shingles (Herpes zoster)	B02	053
Tetanus (lockjaw)	A35	037
Norovirus	A0811	00863
Polio	A80	045
Meningococcal disease	A390, A3950–A3953, A3981–A3984, A3989, A399	036
Hepatitis	B15–B19	AHRQ 6
Hepatitis A	B15	–
Hepatitis B, acute	B16	–
Other acute hepatitis	B17	–
Chronic viral hepatitis	B18	–
Unspecified hepatitis	B19	–
Ebola	A984	0658, 07889
Skin infections (impetigo, abscess, cellulitis)	L00–L039, L08	AHRQ 197, 684
Intestinal infections	A08–A09	AHRQ 135
Enteritis	K529	5589
Lyme disease	A6920	08881

AHRQ, Agency for Healthcare for Research and Quality; CM, Clinical Modifications; ICD, International Classification of Diseases.

Table 2. Prevalence of Infectious Conditions of Interest Among Cases vs Controls

Infection type	DS sample (n=6078)	Controls (n=30,326)	OR (95% CI)	*P*[a]
Respiratory				
Coronaviruses (excludes COVID-19)	0	1	–	1.0000[b]
Diphtheria	0	0	–	–
Influenza	128	1010	0.62 (0.52, 0.75)	<0.0001
Haemophilus influenzae type B	0	0	–	–
Measles	3	3	4.99 (1.01, 24.74)	0.0626[b]
Mumps	0	6	–	0.5981[b]
Rubella (German measles)	2	2	4.99 (0.70, 35.44)	0.1323[b]
Whooping cough (pertussis)	1	19	0.26 (0.04, 1.96)	0.2321[b]
Strep pharyngitis	116	2027	0.27 (0.22, 0.33)	<0.0001
Upper respiratory infection	756	8384	0.37 (0.34, 0.40)	<0.0001
Sinusitis	387	4616	0.38 (0.34, 0.42)	<0.0001
Tonsillitis	314	2624	0.58 (0.51, 0.65)	<0.0001
Laryngitis	148	902	0.81 (0.68, 0.97)	0.0218
Bronchitis	236	2334	0.48 (0.42, 0.56)	<0.0001
Scarlet fever	7	96	0.36 (0.17, 0.78)	0.0070
Otitis media	564	3541	0.77 (0.70, 0.85)	<0.0001
Pneumonia	746	993	4.13 (3.74, 4.56)	<0.0001
Aspiration	126	61	10.50 (7.73, 14.28)	<0.0001
Viral	60	23	13.14 (8.12, 21.26)	<0.0001
Bacterial	87	93	4.72 (3.52, 6.33)	<0.0001
H. influenzae-caused	11	8	6.87 (2.76, 17.09)	<0.0001
Pneumococcal	2	0	–	0.0279[b]
Unspecified/Atypical	596	868	3.69 (3.31, 4.11)	<0.0001
Sexually transmitted				
Bacterial vaginosis	32	1128	0.14 (0.10, 0.19)	<0.0001
Chlamydia	1	68	0.07 (0.01, 0.53)	<0.0001[b]
Gonorrhea	7	55	0.63 (0.29, 1.39)	0.2533
Genital herpes	4	255	0.08 (0.03, 0.21)	<0.0001[b]
HIV/AIDS	5	80	0.31 (0.13, 0.77)	0.0074
Human papillomavirus	16	224	0.35 (0.21, 0.59)	<0.0001
Pelvic inflammatory disease	5	85	0.29 (0.12, 0.72)	0.0045
Syphilis	5	45	0.55 (0.22, 1.40)	0.2039
Trichomoniasis	1	62	0.08 (0.01, 0.58)	0.0003[b]
Urinary tract infection	2	25	0.40 (0.09, 1.68)	0.2992[b]
Other infection				
Otitis externa	193	582	1.68 (1.42, 1.98)	<0.0001
Infectious mononucleosis	8	124	0.32 (0.16, 0.66)	0.0010
Zika	0	0	–	–
Shingles (Herpes zoster)	17	322	0.26 (0.16, 0.43)	<0.0001
Tetanus (lockjaw)	0	1	–	1.0000[b]
Norovirus	2	3	3.33 (0.56, 19.92)	0.1968[b]
Polio	0	3	–	1.0000[b]
Meningococcal disease	0	0	–	–
Hepatitis	42	189	1.11 (0.79, 1.55)	0.5435
Hepatitis A	4	12	1.66 (0.54, 5.16)	0.3257[b]
Hepatitis B, acute	4	19	1.05 (0.36, 3.09)	1.0000[b]
Other acute hepatitis	1	6	0.83 (0.10, 6.91)	1.0000[b]
Chronic viral hepatitis	26	120	1.08 (0.71, 1.65)	0.7180
Unspecified hepatitis	6	75	0.40 (0.17, 0.92)	0.0248
Ebola	0	0	–	–
Skin infections (impetigo, abscess, cellulitis)	1035	3201	1.74 (1.62, 1.88)	<0.0001
Intestinal infections	65	639	0.50 (0.39, 0.65)	<0.0001
Enteritis	131	1277	0.50 (0.42, 0.60)	<0.0001
Lyme disease	4	16	1.25 (0.42, 3.73)	0.7622[b]

[a]*Statistical significance was reached at an alpha of <0.05.*

[b]*Fisher's exact test P-value was interpreted due to low sample count.*

DS, Down syndrome; OR, odds ratio.

[0.01, 0.58]; P=0.0003). The DS cohort also had less frequently diagnosed infectious mononucleosis (OR: 0.32 [0.16, 0.66]; P=0.0010); shingles (OR: 0.26 [0.16, 0.43]; P=0.0248); unspecified hepatitis (OR: 0.40 [0.17, 0.92]; P=0.0248); intestinal infection (OR: 0.50 [0.39, 0.65]; P<0.0001); and enteritis (OR: 0.50 [0.42, 0.60]; P<0.0001).

DISCUSSION

Generally, our findings support similar data of this range and magnitude available from previous research.[13] Individuals with DS had lower prevalence of most respiratory infections but, consistent with other findings, higher prevalence of the more severe infections of pneumonia.[14-16] Immune defects and airway anatomical abnormalities, and an inability to handle secretions, have been noted to explain increased infections among individuals with DS.[14] Furthermore, encounter-level provider documentation habits could explain discrepancies; specifically, if a condition that may be assessed as more severe (eg, pneumonia) or as a complication of an initial infection is diagnosed, then less severe or initial conditions (eg, influenza, sinusitis, laryngitis) may be left undocumented.

Specific to STIs, individuals with DS in our study had lower prevalence, most to a statistically significant degree, which could be due to less sexual activity contributed to by noted delays in sexual maturity.[17] Overall, there are limited data on sexual activity of individuals with intellectual disabilities, including individuals with DS, as data are often reported by caregivers rather than the individual with DS and providers are less likely to test this population based on perceived risk, potentially further affecting findings.[18-20]

Recent research among ambulatory and hospitalized adults with DS concluded that, despite an overall low rate of infections among ambulatory patients, hospitalized adults were mostly admitted for infections and that infections were associated with neurological degeneration and increased mortality.[21] Furthermore, specific to the COVID-19 virus, the small group of individuals with DS hospitalized for COVID-19 displayed more severe cases than controls, particularly an increased incidence of sepsis and mechanical ventilation.[22] Additional research to understand unique prevalence of varying infections and subsequent unique effects on individuals with DS is necessary.

Strengths/Limitations

Our DS cohort is one of the largest to date, making it suitable for the analysis of relatively rare morbidities of interest. Incorporating the earliest available patient data, which represented a 28-year span, allowed for a comprehensive look at prevalence. Our analysis also included a large group of controls matched by age and sex, a sample that can be viewed as representative of a U.S. patient population without DS. Differences in race, ethnicity, and insurance should be noted, as these differences may have been contributors to or effects of findings, or both.

While findings represent data from only a single health system, such a large system may provide the most accurate and available review of prevalence nationally, given the United States' fragmented storage of patient data. Furthermore, much of the dataset was drawn from a specialized care center specifically serving adults with DS, which may improve diagnostic accuracy of ICD coding and subsequent prevalence findings. A minority of data came from other nonspecialized system sites less familiar with serving adults with DS, potentially affecting diagnostic consistency. It should be noted that diagnostic accuracy in general can be difficult with individuals with DS for a variety of reasons.[23] While the conditions of interest in this study incorporated an established coding framework of ICD codes[24] and were carefully chosen and reviewed by a physician who specializes in treating DS, it must be acknowledged that the utilized codes may not be ones most commonly used to diagnose conditions among patients with DS, introducing the potential for underrepresentation of conditions. It is also possible that these codes could over- or underrepresent diagnoses among individuals with DS relative to those without DS.

This study looked at all individuals with DS, including youth and adults, and reported prevalence of conditions among them relative to controls. Future longitudinal analyses are necessary to look at conditions across time, to report on youth and adults separately, and to track the course of conditions seen at different life stages of individuals with DS, particularly as the average lifespan continues to increase.

CONCLUSIONS

This follow-up report to a previously published general prevalence study among individuals with Down syndrome[1] drills down specifically into infectious diseases. Among one of the largest known DS cohorts with matching controls in the United States, diagnosis of numerous infectious disease conditions significantly differed between those with and without DS. In particular, pneumonias were more prevalent and sexually transmitted infections less prevalent in individuals with DS. Findings can be used to better inform and guide both primary and specialized practitioners in the screening and treatment of this unique patient population.

Patient-Friendly Recap

- Authors used longitudinal data from patient records at a single health system to compare rates of relatively common infectious diseases in those with Down syndrome (DS) versus a control cohort of similar patients without DS, documenting diagnosis of infections as more or less prevalent.
- Individuals with DS were significantly more likely to have pneumonias and skin infections and less likely to have most other respiratory (eg, influenza, bronchitis, sinusitis) or sexually transmitted infections than their age- and sex-matched counterparts.
- Differing infectious disease prevalences can be used to guide primary and specialized practitioners in the screening, diagnosis, and care of people with DS.

Author Contributions

Study design: Fitzpatrick, Rivelli, Jia, Rzhetsky, B. Chicoine. Data acquisition or analysis: Fitzpatrick, Rivelli, Chaudhari, L. Chicoine, B. Chicoine. Manuscript drafting: Fitzpatrick, Rivelli, Chaudhari, L. Chicoine, B. Chicoine. Critical revision: Fitzpatrick, Rivelli, Chaudhari, L. Chicoine, B. Chicoine.

Conflicts of Interest

None.

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