**Serologic Protection to Routine Vaccinations in Children**

**with Inflammatory Bowel Disease**

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**Abstract**

Background: Treatment for inflammatory bowel disease [IBD] frequently involves the aggressive use of immunosuppressants that increases susceptibility to and severity of other infections. Consequently, many individuals postpone or refuse immunizations due to unstable disease activity and of fear of disease exacerbation. The aim was to evaluate serologic protection to and completeness of routine vaccinations in children with IBD.

Methods: In this single-center cross-sectional study, children with IBD followed at the Alberta Children's Hospital were recruited from September 15, 2011 to August 15, 2012. Demographic data, IBD medication use, infection risk factors, and vaccination records were collected. Serum was also collected for rubella, hepatitis A virus [HAV], and hepatitis B virus [HBV] serology and analyzed by the Provincial Laboratory of Public Health. From review of vaccination records, the proportion with complete series for each vaccine according to the Alberta schedule (at age of vaccination) was evaluated.

Results: 155 children with IBD (93 Crohn’s disease, 46 ulcerative colitis, 16 IBD-unclassified) underwent serum collection; complete vaccine records were available for 152 of these children. At enrolment, 93 subjects (60%) were currently using immunosuppressive medications (systemic corticosteroids n=20; immunomodulators n=70; and biologic n=48); an additional 30 subjects had a past history of immunosuppressive medication use.

Of 155 participants, 69.7% had up to date MMR, DTap-IPV-Hib, and HBV immunizations. Of 152 participants, 81.9% mounted serologic protection to rubella; 20.6% to hepatitis A, and 65.8% to hepatitis B. Of those who had completed the specific vaccinations, serologic immunity was mounted by 113 of the 142 participants (79.6%) to rubella, 79 of the 114 participants (69.3%) to HBV, and 100% of the participants to HAV.

Conclusions: Children with IBD are at risk for vaccine-preventable illnesses due to lack of receiving complete vaccine series and mounting an inadequate serologic response to vaccinations. Therefore, clinicians caring for patients with IBD should be conscientious about adherence to recommended vaccination schedules, measurement of immune response to vaccines, and administering booster vaccinations where appropriate.

**Introduction**

Inflammatory bowel disease (IBD) is a chronic relapsing and remitting condition of inflammation in the gastrointestinal tract. It is an immune-mediated disease resulting from an inappropriate inflammatory response to an environmental stimulus in a genetically susceptible host. Though IBD affects individuals of all ages, some of the manifestations unique to children include severe malnutrition and impaired growth.([[1]](#endnote-1)) IBD affects 70 per 100 000 children with 4.7 per 100 000 new cases in children per year in North America and Western Europe, the regions of highest prevalence.([[2]](#endnote-2),[[3]](#endnote-3))

Treatment for IBD frequently involves the use of potent immunosuppressants to reduce intestinal inflammation, limit complications and induce and maintain remission. Specifically, immunosuppressants, such as systemic corticosteroids (prednisone, methylprednisolone, and budesonide), immunomodulators (azathioprine, 6-mercaptopurine, methotrexate, and thalidomide), calcineurin inhibitors (tacrolimus and cyclosporin), and anti-tumor necrosis factor alpha (anti-TNFα) biologics (infliximab and adalimumab) effectively treat and prevent flare-ups. However, these more aggressive treatments have risks, including increased susceptibility to and severity of infections. Therefore, patients on immunosuppressants should be protected appropriately with vaccines. However, immunosuppressive medications may impair the body’s ability to successfully build an immunogenic response to vaccinations. The health care maintenance of immunocompromised individuals is unique due to the balance of protection against vaccine-preventable diseases and the risk of vaccine adverse events in an immunosuppressed individual. Immunosuppressed individuals with IBD are encouraged to adhere to the same vaccination schedules recommended for the general population with live agent vaccines as the only exception. Canada’s universal health care plan provides all legal residents free access to health services including routine childhood immunizations. The 7th edition of the Canadian Immunization Guide provides specific immunization recommendations for individuals who are medically immunosuppressed for chronic inflammatory conditions like IBD.([[4]](#endnote-4)) The general principles include:

 [1] Assume all individuals are susceptible except if serologic tests prove otherwise.

 [2] Avoid immunizations during periods of altered immunity. If appropriate, vaccination and immunosuppression schedules should be modified to optimize vaccine response.

 [3] Boost aggressively as altered immunocompetence may decrease the magnitude and duration of vaccine-induced protection.

 [4] Unless data is available to support their use, postpone live attenuated vaccines until immune function has improved due to the risks of vaccine-associated infections.

However, in spite of these guidelines, many individuals continue to postpone or refuse all forms of immunizations due to unstable disease activity or because of fear of disease exacerbation. The childhood immunization schedule varies between provinces in Canada. The schedule for the province of Alberta is outlined in Table 1.([[5]](#endnote-5)) In the last decade, additions to the Alberta schedule included Varicella vaccine (2001), Pneumococcal conjugate vaccine (Pneumococcal conjugate vaccine - 7-valent: 2002, Pneumococcal conjugate vaccine - 13-valent: 2010), Meningococcal-C conjugate vaccine (2002), Meningococcal Conjugate Vaccine (Groups A, C, W-135, and Y: 2011), and Human papilloma virus vaccine (2008).

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| **Table 1: Alberta Childhood Vaccination Schedule**  |
| **Age**  | **Vaccine** |
| 2 months  | • DTaP-IPV-Hib1 |
| • Pneumococcal conjugate (PCV13) |
| • Meningococcal conjugate (Men C) |
| 4 months | • DTaP-IPV-Hib |
| • Pneumococcal conjugate (PCV13) |
| • Meningococcal conjugate (Men C) |
| 6 months | • DTaP-IPV-Hib |
| • Pneumococcal conjugate (PCV13) (for high risk children only) |
| ≥ 6 months  | • Influenza2 |
| 12 months | • MMRV3 |
| • Meningococcal conjugate (Men C) |
| • Pneumococcal conjugate (PCV13) |
| 18 months | • DTaP-IPV-Hib |
| 4–6 years | • DTaP-IPV4 |
| • MMR |
| • Pneumococcal conjugate (PCV13) only for children up to 71 months (catch up program) |
| Grade 5 | • Hepatitis B (3 doses) |
| • HPV5 (3 doses for females) |
| Grade 9 | • dTap6 |
| • HPV (Only female students for three years, from Sept. 2009 to June 2012: catch up program) |
| • MCV47  |
| Government of Alberta Health and Wellness, updated August 1, 2012 (5)([[6]](#endnote-6))1 Diphtheria, tetanus, acellular pertussis, polio, *haemophilus influenzae* type b2 Annually, during influenza season 3 Measles, mumps, rubella, and varicella 4 Diphtheria, tetanus, acellular pertussis, polio 5 Human papilloma virus 6 Diphtheria, tetanus, acellular pertussis 7 Meningococcal Conjugate Vaccine (Groups A, C, W-135 and Y)  |

In children with IBD, the completeness of routine childhood vaccinations along with the presence and duration of serologic protection to routine childhood vaccines are unknown. The relationship between immunosuppressive therapy at time of or after vaccination on duration of serologic protection is also unknown. Knowledge of the presence and duration of serologic protection to immunizations in children with IBD may help guide potential future recommendations for routine and booster vaccinations to optimize protection against vaccine- preventable illnesses. This information is especially important for children with IBD at risk for increased incidence and severity of infections due to medical immunosuppression. In addition, knowledge of the trends for incomplete vaccinations will be a valuable asset for health care providers seeking to optimize vaccinations completeness in children with IBD. The objective of this study is to evaluate the serologic protection to and completeness of routine childhood vaccinations in children with inflammatory bowel disease.

**Methods and Materials**

**Participants**

Participants for this single-center cross-sectional study were recruited from September 15, 2011 to August 15, 2012 through the Paediatric Gastroenterology clinic at the Alberta Children’s Hospital. Potential subjects were identified through nonprobability convenience sampling and enrolled by mail, telephone, or in person at the time of a visit. Individuals who had previously participated in the 2008 study “Immunogenicity and Safety of Influenza Vaccine in Children with Inflammatory Bowel Disease” (Ethics ID 21876) were also recruited. The inclusion criteria for the IBD cohort were a diagnosis of IBD disease established by accepted criteria for endoscopy, histology, clinical course, radiology, and surgery(6)([[7]](#endnote-7)) and age between 2 to 18 years. The exclusion criterion was parent or legal guardian unwilling or unable to provide signed informed consent. Subjects were not paid to participate.

**Study Conduct**

Demographic data and medical history were collected from subjects using a standardized questionnaire. This included information about IBD history (IBD type, date of diagnosis, and start and end date of all IBD medications). The IBD medications considered to be immunosuppressive included: systemic corticosteroids (prednisone, methylprednisolone, and budesonide), immunomodulators (azathioprine, methotrexate, and thalidomide), calcineurin inhibitors (tacrolimus and cyclosporin), and anti-TNFα biologics (infliximab and adalimumab).

Data was also collected on infectious history for varicella (chickenpox) infection (date of infection and parental recall versus physician diagnosis versus laboratory confirmation) and risk factors for hepatitis B infection (country of birth, ethnicity, history of jaundice or liver disease, international travel, household exposure to individuals with hepatitis B, blood transfusions, percutaneous risk factors [intravenous drug use, tattoos and body piercings], and nosocomial risk factors [needle stick injury]).

A copy of immunization records was obtained from either the Public Health Clinic or from personal immunization cards. A vaccine dose was considered valid if the written record documented the type of vaccine and date of administration. Invalid records included parental recall without documentation of the type and date of vaccine administration Written informed consent was obtained from each subject and permission was obtained to access immunization records and medical record shadow charts from the Paediatric Gastroenterology clinic to confirm collected data.

Serum was collected (3-5 mL in a gold-top Vacutainer tube) from each subject to assess for serologic protection. This was frequently done in conjunction with other routine IBD investigations or at the start of an intravenous line. In addition to collecting new serum from patients, consent was obtained from subjects who had previously participated in the 2008 study “Immunogenicity and Safety of Influenza Vaccine in Children with Inflammatory Bowel Disease” (Ethics ID 21876) to use the residual serum volume for testing.

**Immunization Completeness**

Patient immunization records were compared with the routine immunization schedule provided by the Government of Alberta Health and Wellness to determine completeness of immunizations. Criterion for up to date immunizations were: (4,5)

* Measles, mumps and rubella vaccine (MMR)- 2 doses (at 12 months and 4-6 years)
* Diphtheria, tetanus, acellular pertussis, inactivated polio virus vaccine and-*Haemophilus influenzae* type b conjugate vaccine(DTaP-IPV-Hib)- 5 doses (at 2 months, 4 months, 6 months, 18 months, 4–6 years [except Hib])
* Hepatitis B vaccine (HBV)- 3 doses (at grade 5 or 9 to 11 years)
* Hepatitis A vaccine (HAV)- 2 doses (6-12 months apart)
* Varicella vaccine (VZV)- 1 dose (if aged 12 months to 12 years old) or 2 doses (28 days apart if greater than 13 years of age)
* 13-Valent pneumococcal conjugate vaccine (PCV13)- 1 dose (if greater than 23 months of age) or 3 doses (if aged 2 to 23 months)
* Meningococcal C conjugate vaccine (Men-C)- 1 dose (if greater than 12 months of age) or 2 doses ( if aged 2 to 12 months)
* Human papilloma virus vaccine (HPV)- 3 doses (females at grade 5 or 9 to 11 years starting in 2008 or at grade 9 or 13 to 15 years from 2009 to 2012)

In the last decade, the Albertan schedule added the Varicella vaccine, Pneumococcal conjugate vaccine, Meningococcal-C conjugate vaccine, and Human papilloma virus vaccine. The majority of the study participants received vaccines under the recommended immunization schedule that only included the: [1] measles, mumps, and rubella vaccine (MMR), [2] diphtheria, tetanus, acellular pertussis, inactivated polio virus vaccine and *Haemophilus influenzae* type b conjugate vaccine (DTaP-IPV-Hib), and [3] hepatitis B vaccine (Hep B); these three vaccines constituted the standard childhood immunizations for assessing completeness of vaccinations.

**Serologic Protection**

The Provincial Laboratory for Public Health (Microbiology), Calgary, Alberta, stored the serum at -20°C and conducted the serologic testing. Antibodies to hepatitis B surface antigen, hepatitis A virus, and rubella were measured by microparticle enzyme immonoassays for the viruses. The assays for hepatitis A virus was qualitatively reported as positive, indeterminate, or negative; a positive result indicated serologic protection. The assays for rubella IgG antibody and antibody to hepatitis B surface antigen were quantitative and were reported in IU/ml and IU/L, respectively. According to Calgary Laboratory Services, serological protection for rubella is indicated by a rubella IgG titer ≥ 15 IU/ml and an antibody titer ≥ 10 IU/L for hepatitis B surface antigen. (7)([[8]](#endnote-8)) Only the results from Rubella, Hepatitis A, and B will be available in this report as the results for varicella zoster virus, measles, mumps, Corynebacterium diphtheria toxin, and Clostridium tetani toxin are pending.

The laboratory technicians and virologists performed the serologic testing without knowledge of the participant’s diagnosis, immune status, or medical treatment.

**Statistical Analysis**

Data was entered into a database with Excel XP (Microsoft Corp, Redman, WA) and statistical analysis was performed using Intercooled Stata software (Stata Corporation, College Station, Texas). We described demographic characteristics, IBD history and immunization completeness. For each vaccine, the proportion of children with IBD with serologic protection was calculated. For vaccine completeness, the proportion of children with IBD and complete routine childhood vaccinations was evaluated.

The Alberta Children’s Hospital Paediatric Gastroenterology Clinic follows approximately 200 children with IBD. Attempts to contact all of these children over the enrolment period were made by mail, telephone, or clinic/hospital visit.

**Results**

**Study Participants**

There were 155 patients who enrolled in the study and provided serum; 93 Crohn’s disease, 46 ulcerative colitis, and 16 IBD-unclassified. Complete vaccine records were available for 152 of these children. The median age at enrolment was 15.9 years (Table 2).

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| **Table 2. Baseline Characteristics and Risk Factors** |
|  |  | Total Cohort |  | Immunizations UTD |   | Immunizations Not UTD |
| Characteristics | *n* =155 |   | *n* =106 |   | *n* =46 |
| Inflammatory bowel disease type, *n* (%) |  |  |  |  |  |  |
|  | Crohn's disease | 93 | (60.0%) |  | 65 | (61.3%) |  | 26 | (56.5%) |
|  | Ulcerative colitis | 46 | (29.7%) |  | 31 | (29.2%) |  | 14 | (30.4%) |
|  | Indeterminate colitis | 16 | (10.3%) |  | 10 | (9.4%) |  | 6 | (13.0%) |
| Sex, *n* (%) |  |  |  |  |  |  |
|  | Male | 83 | (53.5%) |  | 56 | (52.8%) |  | 26 | (56.5%) |
|  | Female | 72 | (46.5%) |  | 50 | (47.2%) |  | 20 | (43.5%) |
| Median diagnosis age in years (Q1, Q3) | 12.1 | (9.0, 14.5) |  | 12.6 | (9.5, 14.6) |  | 10.5 | (7.2, 13.8) |
| Median current age in years (Q1, Q3) | 15.9 | (12.8, 17.6) |  | 16.3 | (13.7, 17.7) |  | 14 | (11.5, 16.9) |
| Medically Immunocompromised, *n* (%) |  |  |  |  |  |  |
|  | Any immunosuppressant use | 123 | (79.4%) |  | 81 | (76.4%) |  | 39 | (84.8%) |
|  | Current immunosuppressant use | 93 | (60.0%) |  | 61 | (57.5%) |  | 30 | (65.2%) |
|  | Any corticosteroid use | 105 | (67.7%) |  | 70 | (66.0%) |  | 32 | (69.6%) |
|  | Current corticosteroid use | 20 | (12.9%) |  | 13 | (12.3%) |  | 5 | (10.9%) |
|  | Any immunomodulator use | 98 | (63.2%) |  | 67 | (63.2%) |  | 31 | (67.4%) |
|  | Current immunomodulator use | 70 | (45.2%) |  | 47 | (44.3%) |  | 23 | (50.0%) |
|  | Any biologics use | 59 | (38.1%) |  | 37 | (34.9%) |  | 20 | (43.5%) |
|  | Current biologics use | 48 | (31.0%) |  | 30 | (28.3%) |  | 16 | (34.8%) |
| Chicken pox risk factors, *n* (%) |  |  |  |  |  |  |
|  | Previously infected | 87 | (56.1%) |  | 62 | (58.5%) |  | 23 | (50.0%) |
|  | Vaccinated | 62 | (40.0%) |  | 42 | (39.6%) |  | 18 | (39.1%) |
|  | No vaccinations/infection | 10 | (6.5%) |  | 5 | (4.7%) |  | 5 | (10.9%) |
| Hepatitis B risk factors, *n* (%) |  |  |  |  |  |  |
|  | Caucasian | 107 | (69.0%) |  | 74 | (69.8%) |  | 31 | (67.4%) |
|  | Born in Canada | 140 | (90.3%) |  | 100 | (94.3%) |  | 39 | (84.8%) |
|  | Jaundice | 30 | (19.4%) |  | 20 | (18.9%) |  | 10 | (21.7%) |
|  | Liver disease | 7 | (4.5%) |  | 6 | (5.7%) |  | 1 | (2.2%) |
|  | Travel outside Canada | 131 | (84.5%) |  | 90 | (84.9%) |  | 39 | (84.8%) |
|  | Household exposure to Hep B | 3 | (1.9%) |  | 3 | (2.8%) |  |  | 0 |
|  | Blood transfusion | 22 | (14.2%) |  | 11 | (10.4%) |  | 9 | (19.6%) |
|  | Needle stick injury | 1 | (0.6%) |  |  | 0 |  | 1 | (2.2%) |
|  | Body piercings | 49 | (31.6%) |  | 39 | (36.8%) |  | 10 | (21.7%) |
|   | Tattoos | 3 | (1.9%) |   | 3 | (2.8%) |   |   | 0 |
| UTD, up to date; standard immunizations: measles, mumps, and rubella vaccine, diphtheria, tetanus, acellular pertussis, inactivated polio virus vaccine, and *Haemophilus influenzae* type b conjugate vaccine; Q1, first quartile; Q3, third quartile; 3 participants did not have valid documentation of immunization records |

**Immunosuppressive Medication Use**

At enrolment, 93 participants (60.0%) were on immunosuppressive therapy: 20 on systemic corticosteroids (15 on prednisone, 2 on methylprednisolone, and 3 on budesonide); 70 on immunomodulators (41 on azathioprine, 28 on methotrexate and 1 on thalidomide); and 48 on biologics therapy (45 on infliximab and 3 on adalimumab). Of these patients on immunosuppressive therapy, 41 participants (44.1%) were on combination therapy: 9 on corticosteroids and immunomodulators; 2 on corticosteroids and biologics; 26 on immunomodulators and biologics; and 4 on corticosteroids, immunomodulators, and biologics. Participants with Crohn’s disease (74.2%) were more likely to be on immunosuppressants than either ulcerative colitis (34.8%) or IBD- unclassified (50.0%).

A total of 123 participants (79.4%) reported having ever used immunosuppressants: 105 used systemic corticosteroids (104 used prednisone, 9 used methylprednisolone, and 10 used budesonide); 98 used immunomodulators (88 used azathioprine, 43 used methotrexate, and 1 used thalidomide); and 59 used biologics (58 used infliximab and 3 used adalimumab).

From review of the 152 vaccination records, the proportion with complete series for each vaccine according to the Alberta schedule (at age of vaccination) was evaluated. 106 participants (69.7%) had the standard immunizations up to date: 142 participants (93.4%) for MMR, 130 participants (85.5%) for DTap-IPV-Hib, and 127 participants (83.6%) for HBV (Table 3). For the HPV vaccinations, 126 participants (82.9%) did not receive the vaccine: 25 female participants did not receive the vaccine, 20 female participants were outside of the appropriate age bracket and 82 male participants were excluded from the numbers for HPV. Of note, 1 of the 82 male participants with valid immunization documentation received the HPV vaccine. Only 87 participants (56.1%) had a history of chicken pox, of these 51 participants reported diagnoses by a physician and 10 cases were confirmed by a blood test. For varicella, 60 participants received at least one dose of varicella vaccine; 87 non-vaccinated participants had a history of chickenpox infection. However 10 of 152 participants had neither been infected nor vaccinated, including 7 participants who were currently using immunosuppressive medications.

At this time, serology results are only available for rubella, hepatitis B, and hepatitis A. Of 155 participants, 127 participants (81.9%) demonstrated serologic immunity to rubella, 102 participants (65.8%) had serologic immunity to hepatitis B virus, and 32 participants (20.6%) had serologic immunity to hepatitis A virus. Though 139 participants completed the MMR series, 26 of these subjects lacked serologic protection to rubella, including 15 subjects who were currently using immunosuppressive medications.

For hepatitis B, 150 participants (96.7%) had at least one known risk factor. Twenty-two (14.2%) reported a history of packed red blood cell transfusion with a total number of 29 transfused units (range 1 to 3). Fourteen participants received no or incomplete vaccine series (not accounted for by age less than recommended age of vaccination). Though 114 subjects completed the HBV series, 33 of these subjects lacked serologic protection to HBV. In total, 57 of 155 (36.8%) participants lacked serologic protection to HBV. In the naive group, potential risk factors for infection included past history of travel outside of Canada (*n*=49), blood transfusion (*n*=8), and body piercing (*n*=15).

For hepatitis A, 9 participants completed the HAV series and all mounted serologic protection. Interestingly, 22 of 137 subjects with no prior HAV vaccination mounted serologic protection to HAV; though 18 of these participants were born in Canada, all 22 participants had travelled outside of Canada.

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| **Table 3. Vaccination Protective Status** |
|  | Up to date |  | Not up to date |
| Vaccinations, *n* (%) | *n* =152 | Complete (series) | Complete for age |   | *n* =152 | No Doses | Partial (Series) |
| MMR | 142 | (93.4%) | 139 | (97.9%) | 3 | (2.1%) |   | 10 | (6.6%) | 5 | (50.0%) | 5 | (50.0%) |
| DTaP-IPV-Hib | 130 | (85.5%) | 73 | (56.2%) | 57 | (43.8%) |   | 22 | (14.5%) | 1 | (4.5%) | 21 | (95.5%) |
| HBV | 127 | (83.6%) | 114 | (89.8%) | 13 | (10.2%) |   | 25 | (16.4%) | 14 | (56.0%) | 11 | (44.0%) |
| HAV | 13 | (8.6%) | 9 | (69.2%) | 4 | (30.8%) |   | 139 | (91.4%) | 137 | (98.6%) | 2 | (1.4%) |
| VZV | 142 | (93.4%) | 60 | (42.3%) | \*85 | (60.0%) |   | 10 | (6.6%) | 10 | (100.0%) |  | 0 |
| PCV13 | 17 | (11.2%) | 16 | (94.1%) | 1 | (5.9%) |   | 135 | (88.8%) | 135 | (100.0%) |  | 0 |
| Men C | 111 | (73.0%) | 111 | (100.0%) |  | 0 |   | 41 | (27.0%) | 36 | (87.8%) | 5 | (12.2%) |
| HPV§ | 41 | (58.6%) | 21 | (51.2%) | 20 | (48.8%) |   | 29 | (41.4%) | 25 | (86.2%) | 4 | (13.8%) |
| Complete (series)- received all scheduled doses; Complete for age- received all doses appropriate for age; No doses- zero doses received; Partial (series)- received ≥1 dose, still missing ≥1 dose; \* 85 participants had previous infection history with 3 also receiving vaccinations; § 70 female participants with valid immunization documentation |

**Discussion**

Only 69.7% of the participants had the standard immunizations (MMR, DTap-IPV-Hib, and HBV) up to date. Nearly a third of individuals in a high-risk group for more frequent and severe infections had not received protection against vaccine- preventable diseases. In general, the individuals with better access to vaccinations and less severe disease course had a greater proportion of the standard immunizations up to date. For the individuals with the standard immunizations up to date, they were in general older at diagnosis (median age of 12.6 versus 10.5 years) and born within Canada (94.3% versus 84.8%). The older age of diagnosis suggests that fewer immunizations may have been deferred as a result of the onset of the disease. As well, in general, children born in Canada have greater accessibility to medical care, increased awareness of immunizations and free routine child immunizations. In comparison, there were several trends suggesting a more severe disease course in the individuals who had not received the standard immunizations. A greater proportion had a history of medical immunosuppression (84.8% versus 76.4%) and had received blood transfusions (19.6% versus 10.4%), Medical immunosuppression may have acted as a deterrent to receiving immunizations, and blood transfusions often indicate a more severe and acute disease course. Of note, there was also an increased prevalence of body piercings and tattoos in individuals with up to date standard immunizations. However, this is most likely corresponding to the greater age of that group and more opportunity to acquire body piercings and tattoos.

Ten participants (6.5%) did not have either previous exposure to the varicella infection or immunizations. The number of children without any serologic protection to the varicella virus is very alarming as infection at an older age tends to be more severe. The low proportion of patients with IBD with up to date vaccinations in general demonstrates the necessity for medical staff and caregivers to address the risk of infections and benefits of immunizations. Adherence to the recommended immunization schedule is especially important for those patients who are medically immunocompromised or at a higher risk of infection.

A high proportion of individuals received the hepatitis B vaccine, nevertheless, only 79 of the 114 vaccinated participants (69.3%) demonstrated serologic immunity. Similarly, rubella also had only 113 of the 142 vaccinated participants (79.6%) demonstrating serologic immunity. However, 32 participants had serologic protection to hepatitis A, although only 13 had received the vaccine. The 19 individuals who demonstrated serologic immunity without receiving hepatitis A vaccinations may have been inadvertently exposed to the virus from traveling outside of Canada.

Although the goal was to enrol 200 participants, 155 underwent serum collection and complete vaccination records were available for 152 participants. The reasons for refusal of study participation included fear of needles and being unable to provide signed informed consent. The serological nature of the study may have resulted in a self-selection bias. As individuals who had a ‘fear of needles’, including blood work and vaccinations, may have declined participation and provided an exaggerated representation of immunization completeness. Thus, the proportion of participant with up to date vaccinations may be a biased representation of the paediatric IBD population.

This study was also limited by the small sample size of the cohort and incomplete immunization data for several of the participants. This study is representative of children elsewhere with similar disease type and treatment; however, even though the participants were managed closely in a multidisciplinary IBD clinic, the data is from a single tertiary-care paediatric hospital.

As well, while enrolment was open to children aged 2 to 18 years old, the majority of participants were over 12 years old. The immunization schedule recommends that most children receive the majority of their vaccines before this age. Therefore, because of a small sample size and immunization schedules for children less than 12 years of age, our findings should be generalized only to children with IBD over 12 years of age.

The pattern of immunogenicity requires further elucidation as the results in this study suggest that medical immunosuppression affects the magnitude and duration of vaccine-induced immunity. Differing vaccination timing relative to immunosuppressive treatment may achieve better immunological protection. Ongoing assessment of the outcomes of aggressive vaccination in immunosuppressed children is essential, as is critical revisions to the recommended vaccination schedule. Further studies on the relationship between vaccine-induced immunity and vaccine completeness in the paediatric inflammatory bowel disease population are warranted.

**Conclusions**

This study provides additional information to the currently available literature on the use of vaccinations in children with IBD. Specifically, this study reinforces the notion that all children with IBD, regardless of medical immunosuppression, should adhere to the recommended schedule (aside from live vaccines) as immunizations decrease the risk of vaccine-preventable illnesses. This risk is due to lack of receiving or completing vaccine series and inadequately mounting appropriate serologic protective response in spite of vaccination. Data suggests that a history of childhood infection and previous complete immunization does not guarantee immunogenic protection. If there is any question as to whether vaccines were administered or were immunogenic, repeating immunizations is a recommended and acceptable option.

The low proportion of participants with complete up to date immunizations demonstrates the need to address the risk of infections from vaccine-preventable diseases in patients with IBD, especially those on immunosuppressive medications. Therefore, clinicians caring for patients with IBD should be conscientious about adherence to recommended vaccination schedules, measurement of immune response and serologic protection to vaccines, and booster vaccinations where appropriate.

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