

Epidemiology of Meckel's diverticulum: A nationwide population-based study in Taiwan

Characteristics of the cases from surgery between 1996 and 2013

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Abstract

The diverse presentation of Meckel's diverticulum (MD) is a diagnostic challenge for clinicians and most previous studies consist of single institutional case series. The aim of this study was to review the related diagnoses of MD and to investigate the epidemiological characteristics using Taiwan's National Health Insurance Research Database.

We conducted an observational study using a population-based database. Patients diagnosed with MD who concurrently received intestinal surgery were identified. We analyzed the patients' demographic characteristics and relevant diagnoses using χ^2 test and 2-sample *t* test.

We identified 2453 newly diagnosed MD patients from 1996 to 2013 and 1227 patients (50%) with intestinal obstruction, gastrointestinal bleeding, and acute appendicitis (acute abdominal pain) were defined as symptomatic. The male to female ratio was 2.4:1 with half of the patients experiencing symptomatic MD before the age of 20 years' old. The age-specific and annual incidence were calculated for all MD and symptomatic MD. Among the symptomatic MD patients, intestinal obstruction was present in 583 (48%), acute appendicitis was present in 464 (38%), and gastrointestinal bleeding was present in 283 (23%) patients. Intestinal obstruction was the most common preoperative diagnosis in the 0 to 10 years and >20 years' age groups, and acute appendicitis (acute abdominal pain) was the most common diagnosis in the 11 to 20 years' age group.

This population-based 18 years' epidemiologic study described the distributions of MD symptoms among different age groups, which may help clinicians gain a better understanding of this diagnostically challenging gastrointestinal anomaly.

Abbreviations: ICD-9-CM = International Classification of Diseases, Ninth Revision, Clinical Modification, MD = Meckel's diverticulum, NHI = National Health Insurance, NHIRD = National Health Insurance Research Database.

Keywords: appendicitis, epidemiology, gastrointestinal bleeding, intestinal obstruction, Meckel's diverticulum

1. Introduction

Meckel's diverticulum (MD), a remnant of the vitelline duct, is the most common congenital anomaly of the gastrointestinal tract with a prevalence of approximately 2 percent in the general

population.^[1,2] Most of the MD are asymptomatic and is usually discovered incidentally by imaging studies^[3] or during abdominal surgery.^[4] There was a rate of 4.2% to 6.4% for developing complications over a lifetime.^[1,5] Age-related differences in

Editor: Kuku Noertjojo.

The authors report no conflicts of interest.

This study is supported in part by Taiwan's Ministry of Health and Welfare Clinical Trial Center (MOHW109-TDU-B-212-114004), the MOST Clinical Trial Consortium for Stroke (MOST 108-2321-B-039-003-), and the Tseng-Lien Lin Foundation, Taichung, Taiwan.

The data that support the findings of this study are available from a third party, but restrictions apply to the availability of these data, which were used under license for the current study, and so are not publicly available. Data are available from the authors upon reasonable request and with permission of the third party.

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How to cite this article: Chang YC, Lai JN, Chiu LT, Wu MC, Wei JC. Epidemiology of Meckel's diverticulum: A nationwide population-based study in Taiwan—characteristics of the cases from surgery between 1996 and 2013. *Medicine* 2021;100:50(e28338).

Received: 29 June 2020 / Received in final form: 26 November 2021 / Accepted: 29 November 2021

<http://dx.doi.org/10.1097/MD.00000000000028338>

presentation have been noted, ranging from incidental finding to intestinal obstruction, bleeding, and inflammation. It is generally thought that children tend to present with intestinal bleeding, whereas adults more commonly present with intestinal obstruction. However, large case series and population-based studies have shown the opposite results.^[4,6] Because previous studies were mostly case series conducted in single institutions and had different definitions of “children” and “adult,” there is presently no consensus on this point. Intestinal obstruction may result from intussusception, volvulus due to fibrous bands, invasive carcinoid tumor, or incarcerated hernia,^[4,7] whereas bleeding is usually caused by small bowel ulceration due to ectopic tissue. Inflammation, mostly diverticulitis, is often the result of obstruction of the diverticular opening due to inflammatory tissue, enterolith,^[8] food or other foreign body,^[9] or tumor, and may lead to perforation and peritonitis. Acute abdominal pain mimicking acute appendicitis is the most common symptom preoperatively.^[10,11] Preoperative diagnosis of MD is challenging. In a case series of 2 tertiary French medical centers, preoperative diagnosis was about 40% and exploratory laparoscopy is often necessary.^[10]

In this study we analyzed Taiwan’s National Health Insurance Research Database (NHIRD), which contains the NHI (National Health Insurance) medical records of almost 99% of the nation’s population of approximately 23 million residents. Thousands of studies in the literature have used the NHIRD to conduct large-scale population-based epidemiological research on specific diseases.^[12] The goals of this study were to explore the epidemiology of MD, and to gain insights into the distributions of age, sex, year incidence, especially with a focus on related diagnoses among MD patients in Taiwan for the period 1996 to 2013.

2. Methods

2.1. Data source

This study was approved by the Research Ethics Committee of China Medical University and Hospital in Taiwan (no. CMUH-104-REC2-115-CR-4). Data from the hospitalization dataset of Taiwan’s NHIRD were used, which included demographic information and national health insurance claims records from 1996 to 2013. All data derived from the NHIRD are de-identified by scrambling the identification codes of both patients and medical facilities for epidemiologic research. The data include patients’ demographics, medical expenses, diagnostic codes (International Classification of Disease, 9th Revision, Clinical Modification [*ICD-9-CM*]), and so forth. The *ICD-9-CM* codes were used to identify diseases of each patient in the dataset.

2.2. Definition of cases

We used inpatient claims data to identify patients with newly diagnosed MD (*ICD-9-CM* code 751.0) for the period 1996 and 2013. Because it was not possible to discriminate between definite and suspected MD cases, we used *ICD-9-CM* procedural codes with concurrent operations on intestine or operation on the abdominal region (*ICD 45, 46 and 54*) to define cases of MD. To assess the distributions of symptoms based on age, patients were stratified into 3 age groups: 0 to 10 years’ old (young children), 11 to 20 years’ old (adolescents), and >20 years’ old (adults). Using *ICD-9-CM* codes diagnoses up to 3 months before MD diagnosis were included in the analysis. Because some MD patients may have deferred their operation after diagnosis, the surgery and

Table 1

The most common ICD-9-CM codes used for diagnoses in this study.

Diagnosis	ICD 9
Gastrointestinal bleeding	578, 562.02, 772.4
Intestinal obstruction	560
Intussusception	560.0
Paralytic ileus	560.1
Volvulus	560.2
Other specified intestinal obstruction	560.8
Acute appendicitis	540–543
Digestive system diseases	520–579 (except 560, 578, 562.02, 540–543)
Other diseases of intestines and peritoneum	562–569 (except 562.02)
Other diseases of digestive system	570–579 (except 578)
Hernia of abdominal cavity	550–553
Diseases of esophagus, stomach, and duodenum	530–539
Neoplasms	140–239
Malignant neoplasm of digestive organs and peritoneum	150–159
Malignant neoplasm of lymphatic and hematopoietic tissue	200–208
Malignant neoplasm of other and unspecified sites	190–199
Congenital anomalies	740–759 (except 751.0)
Digestive system	749–751 (except 751.0)
Circulatory system	745–747
Urinary system	753
Injury and poisoning	800–999
Complications of surgical and medical care	996–999
Intracranial injury	850–854
Effects of foreign body entering through Body orifice	930–939
Blood diseases	280–289
Anemia	280–285
Coagulation/hemorrhage	286–287
Other	288–289

diagnosis may not have been within the same hospitalization. Therefore, data from a 3-month period before MD diagnosis were included in the analysis to gain a clearer understanding of the effects of related factors in each patient. As such, a single MD patient may have had >1 diagnosis and all of these diagnoses were included in the analysis. Almost all of the *ICD-9-CM* codes were used to avoid missing any related diagnoses (Table 1).

The age-specific incidence was calculated as the number of MD diagnoses in a 10-year interval age group divided by the number at risk for that group. The annual incidence rate was calculated as the number of MD diagnoses divided by the population size at risk during each calendar year between 1996 and 2013.

2.3. Statistical analysis

We compared the distribution of demographic characteristics and the top 5 symptoms among MD patients classified by 3 age groups (0–10, 11–20, and >20 years). Demographic characteristics were sex, inpatient days, medical expenses, and postoperative mortality. Categorical variables were presented as numbers with percentages and were analyzed using the χ^2 test. Continuous variables were presented as mean and standard deviation using the 2-sample *t* test. We measured age-specific and annual incidence rates of MD patients with concurrent surgery identified in the database by 100,000 person-years during 1996 to 2013. Two percent of the study population were considered to be at

Table 2
Characteristics of Meckel's diverticulum patients stratified by age groups.

Characteristics	Meckel's diverticulum patients with operations on intestine or abdominal region (n=2453)						P
	age 0–10 y, n=730		age 11–20 y, n=424		age >20 y, n=1299		
	n	%	N	%	n	%	
Sex							<.0001
Female	197	26.99	93	21.93	428	32.95	
Male	533	73.01	331	78.07	871	67.05	
Inpatient days	10.08 ± 9.66		9.48 ± 6.68		12.81 ± 13.29		<.0001
Medical expenses (NTD)	7689.98 ± 97695.18		63307.26 ± 71634.15		96920.79 ± 109621.61		<.0001
Proportion of symptomatic patients	382	52.33	260	61.32	585	45.03	<.0001
Postoperative mortality	3	0.41	0	0.00	33	2.54	<.0001

Data shown as n (%) or mean ± SD (SD=standard deviation).
 Postoperative mortality: death within 30 days after surgery.

risk. Statistical analyses were performed using SAS software, version 9.4 (SAS Institute, Cary, NC). Two-tailed *P* < .05 was considered statistically significant.

3. Results

3.1. Characteristics of the study population

A total of 2453 MD patients who underwent operations on the intestine or the abdominal region (without appendectomy) from 1996 to 2013 were identified. The >20 years age group had a significantly higher number of inpatient days, medical expenses, and postoperative mortality than the other age groups (Table 2). A total of 1227 MD patients had intestinal obstruction, gastrointestinal bleeding, or acute appendicitis and were defined as symptomatic (see later explanation). Patients in the symptomatic group comprised 50% of the total number of MD patients (Table 2).

3.2. Demography of patients

The age-specific and annual incidence rate was calculated by assuming that 2% of the general population had MD. The number of MD patients decreased with age but not the age-specific incidence rate, which initially showed a decline and slightly increased after the age of 70 years (Fig. 1), and ranged from 7.5 to 38.3 per 100,000 person-years for symptomatic MD patients and 16.8 to 73.3 per 100,000 person-years for total MD patients. The annual incidence rate changed little during the study period, which ranged from 10.4 to 18 per 100,000 person-years in the symptomatic group and 23.3 to 35.2 per 100,000 person-years in all MD patients (Fig. 2).

3.3. Age and sex distribution

In total, there were 2453 MD patients and among these, 730 (30%) were 0 to 10 years' old, 424 (17%) were 11 to 20 years'

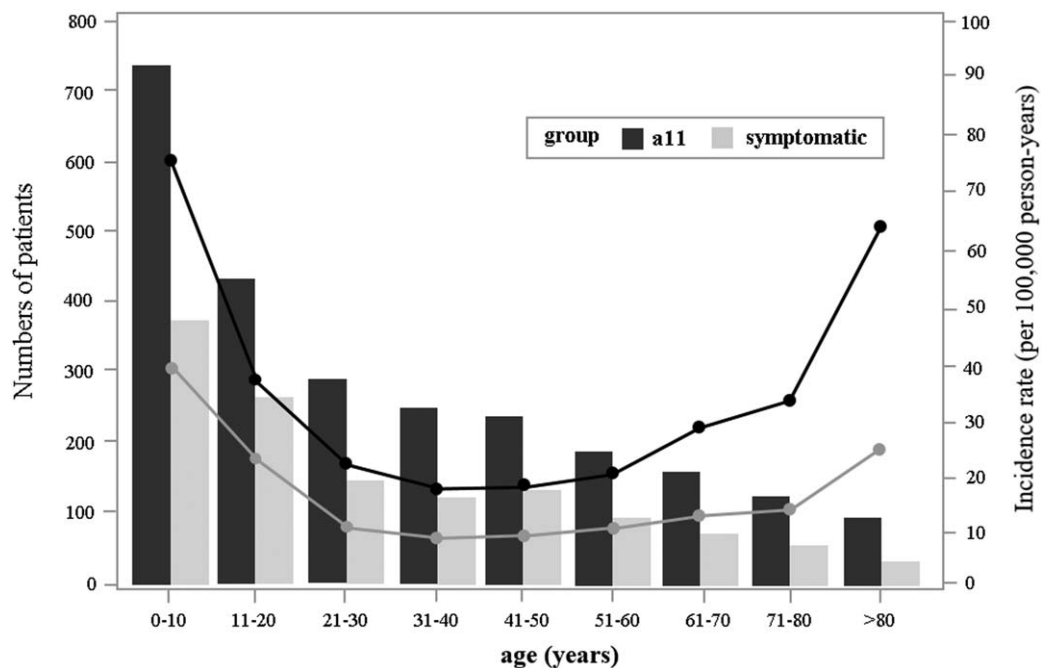


Figure 1. Distribution of Meckel's diverticulum cases for all and symptomatic groups by age and incidence rates (case number per 100,000 person-years).

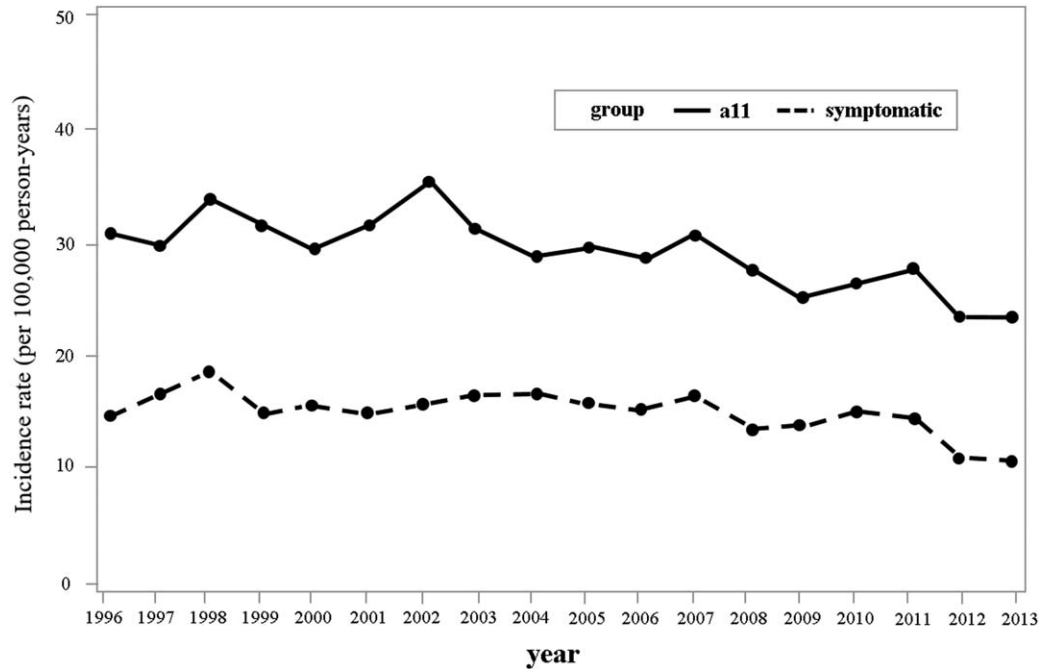


Figure 2. Annual incidence rates (case number per 100,000 person-years) for all and symptomatic Meckel's diverticulum cases from 1996-2013.

old, and 1299 (53%) were >20 years' old. The mean age of all MD patients was 28.6 ± 24.3 years. Seventy-one percent of total MD patients were male, and the male (n = 1735) to female (n = 718) ratio was 2.4:1. Among the 1227 symptomatic MD group, there were 382 (31%), 260 (21%), and 585 (48%) patients, respectively, in the youngest to oldest age groups, and the male (n = 864) to female (n = 363) ratio was 2.4:1. The mean age for symptomatic MD patients was 26.0 ± 26.7 years.

3.4. Clinical presentation

The 5 most common clinical diagnoses in all age groups were intestinal obstruction (23.8%), acute appendicitis (18.9%), digestive system diseases (16%), gastrointestinal bleeding (11.5%), and injury and poisoning (8.3%). However, 12.5% of patients did not have another diagnosis except MD. Details of the related diagnoses in the 3 age groups are illustrated in Tables 3 to 5.

Among the 1227 symptomatic patients, intestinal obstruction was present in 583 (48%), acute appendicitis was present in 464 (38%), and gastrointestinal bleeding was present in 283 (23%) patients. In the different age groups, the frequency of symptoms in the 0 to 10 years' age group (n = 382) was intestinal obstruction (188 patients; 49%, mostly were intussusception and volvulus), gastrointestinal bleeding (164 patients; 43%), and acute appendicitis (60 patients; 16%); in the 11 to 20 years' age group (n = 260), the most frequent diagnoses were acute appendicitis (123 patients, 47%), intestinal obstruction (108 patients; 42%), and gastrointestinal bleeding (61 patients; 23%); and in the >20 years age group (n = 585), intestinal obstruction (287 patients; 49%), acute appendicitis (281 patients; 48%), and gastrointestinal bleeding (58 patients; 10%) were the most prevalent diagnoses.

4. Discussion

This is the first study to analyze nationwide population-based data to describe the epidemiology and related diagnoses of MD in

all ages. The majority of studies on MD and its clinical symptoms are mostly case series or only investigate a specific age group. This is one of the largest population-based studies of MD across all ages and highlights related symptoms in patients diagnosed with MD and their clinical significance.

MD is generally believed to be present in 2% of the general population, so we assumed 2% of the population had MD in our calculations of the age-specific and annual incidence rates. In our data, the age-specific incidence rate ranged from 16.8 to 73.3 per 100,000 person-years (7.5–38.3 per 100,000 person-years in symptomatic group) and male predominance was noted in all age groups. The age-specific incidence rate peaked in the 0 to 10

Table 3

The 5 major diagnoses related to Meckel's diverticulum and its 3 major sub-diagnoses in patients aged 0–10 years (n = 730).

Diagnoses	n	%
Intestinal obstruction	188	25.8
Intussusception	93	12.7
Volvulus	46	6.3
Other specified intestinal obstruction	37	5.1
Gastrointestinal bleeding	164	22.5
Blood diseases	119	16.3
Anemia	95	13.0
Other	9	1.2
Coagulation/hemorrhage	3	0.4
Digestive system diseases	75	10.3
Other diseases of intestines and peritoneum	45	6.2
Other diseases of digestive system	14	1.9
Hernia of abdominal cavity	10	1.4
Congenital anomalies	70	9.6
Digestive system	53	7.3
Circulatory system	11	1.5
Urinary system	4	0.5

Table 4**The 5 major diagnoses related to Meckel's diverticulum and its 3 major sub-diagnoses in patients aged 11–20 years (n=424).**

Diagnoses	n	%
Acute appendicitis	123	29.0
Intestinal obstruction	108	25.5
Other specified intestinal obstruction	56	13.2
Intussusception	31	7.3
Paralytic ileus	16	3.8
Gastrointestinal bleeding	61	14.4
Digestive system diseases	54	12.7
Other diseases of intestines and peritoneum	21	5.0
Other diseases of digestive system	13	3.1
Diseases of esophagus, stomach, and duodenum	11	2.6
Blood diseases	33	7.8
Anemia	26	6.1
Coagulation/hemorrhage	3	0.7
Other	1	0.2

years' age group and gradually declined, and another peak was observed in older age (>70 years' old). The trend was quite similar to that observed in a study by Soltero et al, who found the complication rate of MD peaked at age 0 to 4 years and in patients older than 80 years.^[5] One of the possible explanation for the increased rate for elder people may be the increased incidence of gastrointestinal tumor or MD cancer.^[13] Another population-based study conducted by Cullen et al, who also used 2% of the population to calculate MD complications in Olmsted County, USA, found an average age-specific incidence of 87.4 per 100,000 person-years with female predominance over the age of 60 years.^[11] Another study by Leijonmarck et al in Stockholm, Sweden, who also used 2% as the general incidence of MD, the complication rate of MD was estimated as 0.03 percent per year.^[7] The age-specific incidence rate for symptomatic MD in our study was lower than the 3 studies mentioned above. The lower incidence rate in our study could be explained by a number of possible factors including population ethnicity, study design (the definition of symptomatic MD may underestimate the

Table 5**The 5 major diagnoses related to Meckel's diverticulum and its 3 major sub-diagnoses in patients aged >20 years (n=1299).**

Diagnoses	n	%
Intestinal obstruction	287	22.1
Other specified intestinal obstruction	138	10.6
Volvulus	60	4.6
Paralytic ileus	48	3.7
Acute appendicitis	281	21.6
Digestive system diseases	263	20.2
Other diseases of intestines and peritoneum	135	10.4
Diseases of esophagus, stomach, and duodenum	54	4.2
Other diseases of intestines and peritoneum	36	2.8
Neoplasms	185	14.2
Malignant neoplasm of digestive organs and peritoneum	132	10.2
Malignant neoplasm of lymphatic and hematopoietic tissue	27	2.1
Malignant neoplasm of other and unspecified sites	13	1.0
Injury and poisoning	133	10.2
Complications of surgical and medical care	98	7.5
Intracranial injury	24	1.8
Effects of foreign body entering through Body orifice	9	0.7

incidence of MD), and the observation period. In addition, our incidence rate showed male predominance throughout all ages. The result was also different from Cullen's study, which revealed the age-specific rates were greater in women over the age of 60 years. Despite these inconsistencies, we believe our results may be of value as the reference data and are representative of the epidemiology of MD in Taiwan due to the large number of patients studied and the population-based nature of this investigation.

MD-related acute abdominal pain may result from diverticulitis, bowel obstruction, perforation, or even peritonitis, mimicking the symptoms of acute appendicitis.^[14,15] In a retrospective case series conducted by Chen et al, 24% (56/233) of MD patients with a final diagnosis of diverticulitis or perforated MD were initially suspected of having appendicitis or peritonitis preoperatively. Abdominal pain was present in 87.5% (49/56) of the above cases.^[11] Another retrospective study of adult MD patients by Parvanescu et al showed 100% of MD patients presented with abdominal pain.^[10] Also, it is well known that abdominal pain is reported in nearly all confirmed cases of appendicitis.^[16] Our data, which did not include appendectomy (the ICD-9 CM code of appendectomy is 47), showed that the majority of preoperative diagnoses were appendicitis in the 11 to 20 years' age group (29% in the total MD group and 47% in the symptomatic MD group) and was the second most common diagnosis in the >20 years' age group (21.6% in the total MD group and 48% in the symptomatic MD group). This implies acute abdominal pain is the major complaint resulting from abdominal inflammation in adolescent and adult MD patients. A thorough evaluation and exploration to rule out MD as the source of the patient's symptoms is necessary, especially when the appendix is mildly inflamed or normal.^[17]

Intestinal obstruction and gastrointestinal bleeding are known to be the 2 most common symptoms of MD. Typically, children with MD tend to present with painless rectal bleeding,^[11,18,19] whereas adults with MD more frequently present with intestinal obstruction. However, there are conflicting findings in the literature.^[4,6,20] In a study by Park et al, intestinal obstruction was the predominant symptom in the <10 years' age group, whereas bleeding was the major symptom of the > 11 years age group. Had they defined the pediatric group as <18 years' old, bleeding would be the most common symptom in both pediatric and adult group. Two pediatric population-based studies also revealed intestinal obstruction was the most common presenting symptom.^[6,20] It is difficult to compare symptoms among these studies because of the different categorizations of age groups that were used. Therefore, in the present study, we divided patients into 3 age groups to explore the relationships between age and MD-related symptoms. The results showed that intestinal obstruction, acute abdominal pain, and intestinal obstruction were the most common diagnoses in the 0 to 10, 11 to 20, and >20 years age groups, respectively. If we define pediatric patients as ≤20 years' old, intestinal obstruction would be the most common symptom in both pediatric and adult groups. In addition, the study by Park et al found that younger (especially <4 years) patients tended to present with obstruction rather than bleeding. To observe whether this trend was present in our study, we further analyzed the numbers of the 2 symptoms from 0 to 10 years' old in our study; the data showed the numbers of obstruction was equally greater than bleeding in every single age, no such trend was found. However, the frequency of gastrointestinal bleeding decreased with age, from being the second

common cause of MD in 0 to 10 years' age group to the third common in 11 to 20 years age group (43% and 23%, respectively). If we define pediatric patients as ≤ 20 years' old, gastrointestinal bleeding remains the second common cause in pediatric group but not in adult group, which was only 10% (58/585). The proportion was similar and within the wide range of 8% to 63% as reported in the previous studies.^[10,21]

The proportion of symptomatic MD varies in the literature, and in some of the largest patient series, it ranged from 16% to 60%.^[18] In our study, patients with intestinal obstruction, gastrointestinal bleeding, or acute appendicitis (acute abdominal pain) were defined as symptomatic and constituted 52% (382/730), 61% (260/424), and 45% (585/1299) of the 3 age groups, respectively. The distribution of symptomatic MD was similar to that found in the study by Park et al, with half (642/1227) of the symptomatic group presenting before the age of 20 years. In the symptomatic group, patients younger than 2 years of age comprised only 12% (146/1227) of the total symptomatic patients and 23% (146/642) of symptomatic patients < 20 years in our study, which contradicts the widely accepted "rule of 2," which states that symptomatic MD commonly presents before the age of 2 years.

MD is the most common pathologic lead point of intussusception,^[22] the most common cause of bowel obstruction in infants, and the typical age of occurrence is 5 months to 3 years. In our study, there were 124 intussusception-related MD patients under the age of 20 years. Of the 124 patients, 64 patients were older than 3 years and 7 patients were younger than 5 months, comprising about 57% of the 0 to 20 years population. This implies that an atypical age presentation of intussusception should prompt a thorough evaluation to establish the potential leading point. In adults, intussusception was less common, and fibrous band with or without volvulus was the most common cause of MD-related intestinal obstruction in the past studies.^[7,23]

Anemia from gastrointestinal bleeding of MD may result from ileal ulceration, chronic inflammation, or mucosal irritation from an inverted MD.^[24] Chronic persistent anemia is less commonly seen in MD patients, but sometimes may obscure the underlying MD.^[25] In a study by Suh et al, initial hemoglobin level and symptoms of gastrointestinal bleeding were used to increase the diagnostic accuracy in detecting symptomatic MD.^[26] Another study by Jaramillo et al also used hemoglobin as part of a predictive score to identify children with bleeding MD who may benefit from exploratory surgery without undergoing endoscopy.^[27] In our study, we calculated the "anemia to bleeding ratio" by dividing the number of anemia patients with the number of gastrointestinal bleeding patients and found ratios of 57.9%, 42.6%, and 65.5% in 3 age groups, respectively. This result implies that adults and young children with MD are more vulnerable to anemia resulting from gastrointestinal bleeding and immediate treatment is needed.

Several factors may influence the results of our study. First, we were not able to identify whether the operations were done for MD or other diseases. This seems to be the limitation of such administrative database studies. Second, some symptoms such as chronic abdominal pain were difficult to identify using the ICD codes, which could influence the result of our study. Lastly, we use 2% as the prevalence to calculate age-specific and annual incidences, which was based on the "rule of 2." However, a more recent systemic review found the prevalence to be 1.23% from 31,499 autopsies in 7 studies.^[28] If 1.23% was used to calculate the incidences, the result may be higher than currently calculated.

We still used 2% to calculate to compare the results with other studies.^[1,5,7]

The main strength of this study is that the data were obtained from a large nationwide sample with comprehensive demographics during a defined period of time. However, this study has several limitations. First, all of the data were from hospitalization records, so diagnoses from outpatient and emergency departments were not included. To minimize any error, we included all of the 5 major diagnoses up to 3 months before MD diagnosis. Second, hospital discharge data rely on accurate coding of diagnoses and sometimes inaccurate coding may occur. Third, data in the NHIRD are collected for NHI reimbursement rather than for research purposes and thus do not contain all relevant clinical information, such as laboratory and pathologic results. The symptomatic group in our study may not be representative of true symptomatic MD in the population. Fourth, symptoms such as intestinal obstruction may have been caused by diseases other than MD (eg, intestinal tumor), which may have influenced the accuracy of the results. Fifth, the broad category of ICD coding limited the further analysis of other associated symptoms (eg, types of congenital anomalies or neoplasms). Nevertheless, this is the largest population-based study of all ages in a single country, providing a snapshot of the epidemiology and factors relevant to diagnosis of MD. Our results were partly in line with a recently published population-based data by Friesen et al, who found MD may be more prevalent in adult patients than was previously understood.^[29] We further identified that symptomatic MD in pediatric patients was mostly > 2 years' old, contrary to the previous long-standing beliefs. These findings could provide clinicians more insights in dealing cases with relevant symptoms among those age groups.

5. Conclusion

We found that at least 50% of patients were symptomatic in this observational study and intestinal obstruction was the most common preoperative diagnosis, followed by acute abdomen pain, and gastrointestinal bleeding. Intestinal obstruction was the most common presenting symptom of MD in the 0 to 10 (young children) and > 20 years' (adults) age groups, whereas acute abdominal pain was more common in the 11 to 20 years' (adolescents) age group. Physicians should be aware of the different manifestations in different age groups when a patient presents with ≥ 1 of the aforementioned symptoms and the etiology is uncertain.

Author contributions

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