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Original article

Comparative Incidence of Crohn's Disease Among Age Groups and Its Association with ABO and RhD Blood groups

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Abstract
Crohn's disease (CD) is a chronic inflammatory disorder that impacts the entire gastrointestinal tract, typically diagnosed in individuals during their second or third decade of life. Recent studies have indicated a correlation between ABO blood groups and susceptibility to various diseases. This study aimed to investigate the distribution of ABO and RhD blood groups among patients with CD, as well as the incidence of CD across different age groups. Additionally, it seeks to highlight the role of heredity in the incidence of CD. Samples from 110 CD patients were represented by 60 males (54.5%) and 50 females (45.5%) who attended gastroenterology outpatient clinics at Tripoli University Hospital (TUH) and Tripoli Central Hospital (TCH) for follow-up. Blood samples were serologically screened for ABO and RhD antigens using tube agglutination tests. The most common blood type was blood group O (50%), followed by blood group A (33.6%). Regarding the RhD factor, 87.3% of study subjects were Rhesus positive. In this study, the most frequently occurring CD cases among age groups were found to be among adults (20 to 39 years), with 64.5%, followed by middle-aged adults (40 to 59 years), which was 22.7%. Furthermore, it was determined that 17.3% and 9.1% of affected individuals possess first-degree and second-degree relatives, respectively. Our results established that the O blood group correlates with a heightened risk of developing celiac disease (CD). The age group most affected was between 20 and 39 years.
Keywords. Crohn's disease, RhD factor, ABO blood groups, Age Groups.

Introduction

Crohn's disease (CD) is a chronic inflammatory disorder that affects the entire gastrointestinal tract, extending from the mouth to the anus, with extraintestinal manifestations and associated immune disorders [1]. Depending on the severity of the disease and associated complications, CD is often purely inflammatory, but most patients develop a complicated disease with fistulas and strictures [2]. CD is usually diagnosed in the second or third decade of life at a young age, but it can afflict people of any age [3]. The clinical manifestations of CD disease are diverse and may include poor growth, abdominal discomfort, constipation, diarrhea with blood or mucus, fever, and anemia [4]. Symptoms vary significantly among individuals, posing substantial challenges in developing a standardized diagnostic approach. It is not unusual for patients to experience symptoms for several years before receiving a diagnosis [5].

Laboratory tests are useful to diagnose CD, evaluate disease activity, and determine complications. Initial testing often includes a complete blood count (CBC), BUN, creatinine, liver enzymes, C-reactive protein (CRP), and erythrocyte sedimentation rate (ESR). A stool culture and testing for Clostridium difficile toxin should be considered [6]. Calprotectin and fecal lactoferrin are substitute indicators for bowel inflammation and are utilized for distinguishing between inflammatory conditions and irritable bowel syndrome [7]. The clinical manifestations and post-diagnosis phenotype of CD vary with age. Pediatric-onset CD is more prone to disease compared to the adult and elderly groups. A population-based pediatric study in France found that the location remained stable in over 92% of elderly patients. 31% of pediatric patients had disease extension [8].

Globally, the incidence and prevalence of CD have been significantly rising across all ethnic groups, with annual increases in incidence ranging from 4% to 15% over the past three decades [9]. Studies indicate the highest annual incidence of CD has been recorded in North America (20.2 per 100,000 person-years), followed by Europe (12.7 per 100,000 person-years) and Asia and the Middle East (5.0 per 100,000 person-years). This growing trend has attracted increasing attention from physicians [10].

Scientific evidence clearly points to the role of heredity in IBD. Studies have shown that 5% to 20% of affected individuals have a first-degree relative with one of the diseases [11]. According to one study, 36% of individuals with afflicted parents suffered from IBD [12]. Numerous genes and genetic mutations linked to IBD have been identified. The first one detected was a mutation in the *NOD2/CARD15* gene, which was found to be associated with developing CD. A mutation in the *NOD2/CARD15* gene may be observed in up to 20% of IBD patients in North America and Europe [13].

Recent studies on human microbiota are revealing the critical role of the intestinal bacterial community in the pathogenesis of both systemic and intestinal diseases, including CD. NOD2 plays a key role in the regulation of microbiota in the small intestine. NOD2 is highly expressed in ileal Paneth cells that provide a critical mechanism for the regulation of ileal microbiota by secreting antimicrobial peptides. Therefore, *NOD2* mutations lead to dysregulation of host–microbe interactions, which increases the susceptibility to abnormal ileal inflammation [13].

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Early in the 20th century, Karl Landsteiner discovered that the ABO blood group system was the first genetic feature. The ABO system is divided into four phenotypic groups named A, B, AB, and O. It is associated with the risk of various diseases, such as autoimmune disorders, gastrointestinal malignancies, and cardiovascular diseases [14]. The Rh system emerged as the second most important blood group system due to hemolytic disease of the newborn and its importance in RhD-negative individuals in subsequent transfusions once they develop Rh antibodies [15]. Intestinal disorders and ABO blood groups were previously the subject of a few studies in the 1960s and 1970s, but the findings were controversial [16]. ABO blood group antigens and host-microbe interactions are influenced by FUT2 activity [17]. FUT2 is encoded by the *FUT2* gene, and it is a membrane protein that is responsible for the formation of ABO antigens, their gastrointestinal tract presentations, and body secretions [18]. A substantial correlation was found between the susceptibility to CD and a loss-of-function mutation of the *FUT2* gene. Furthermore, variations in ABO and Galactoside 2-α-L-fucosyltransferase 2 (FUT2) have been identified as risk factors for several illnesses, including CD [19]. However, some studies addressed the potential role of ABO blood groups in IBD development, as a cohort study conducted in Belgium and Italy found no connection between CD risk and ABO variants [20]. Chen et al. confirmed that non-O blood groups were significantly associated with an increased risk of CD in the Chinese Han population [14]. The study aimed to investigate the distribution of ABO and RhD blood groups in CD patients and explore its impact on disease. A secondary objective was studying the differences in the incidence of CD across age and pointing out the role of heredity in CD incidence.

Methods

Study Area and Design

This binary study employed an observational design. It involved 110 patients with CD who attended gastroenterology outpatient clinics at Tripoli University Hospital (TUH) and Tripoli Central Hospital (TCH) for follow-up and biological treatment between January 2024 and March 2024. The inclusion criteria for the study group were patients who had undergone intestinal resection or had a fistula. Patients with a history of malignant tumors or cardiovascular disease were excluded. The study protocol received approval from the Research and Ethics Committees of TUH and TCH. Candidates' medical records and personal interviews with patients using a structured questionnaire were used to gather demographic and clinical data on their gender, year of birth, age at diagnosis, and other medical issues.

Sample collection and blood tests

After obtaining informed consent from 110 CD patients, ABO blood group and RhD factor laboratory investigations were performed. For optimal results, a fresh blood sample was drawn and transferred into ethylenediaminetetraacetic acid (EDTA), and the determination of blood type was performed by a tube agglutination technique.

Data analysis

Statistical analysis was performed using Statistical Package for the Social Sciences (SPSS) software version 27. Descriptive statistics were used to describe the demographic characteristics of the participants. Qualitative data were expressed as percentages and frequencies, while numerical data were presented as mean ± standard deviation. Proportions were created to establish the distribution of blood groups in the study participants.

Results

Demographic data

A total of 110 cases were included in this study, ranging from 10 to 70 years. Among the 100 enrolled patients, 60 (54.5%) were male and 50 (45.5%) were female. The age was 32.57±12.24 years, with a clear predominance of male subjects (Table 1).

Data analysis and interpretation

The prevalence of Crohn's disease across different groups in the studied population revealed that out of 110 respondents, 64.5% were adults aged 20 to 39 years, while 22.7% were middle-aged adults aged 40 to 59 years. The percentage distribution of respondents by age is in Figure 1. Furthermore, the mean age at diagnosis in the study was determined to be 25.92 ± 11.04 years.

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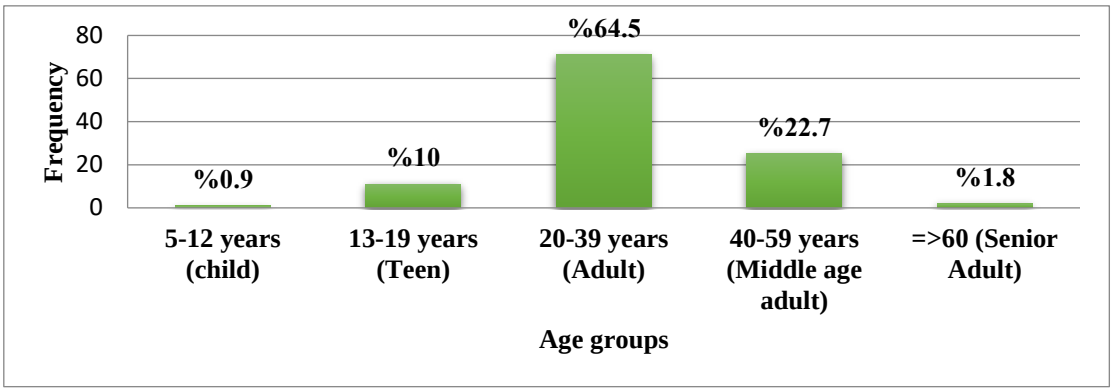

Figure 1. The percentage distribution of respondents in this study according to age

The most prevalent blood type among the study participants was blood group O, accounting for 50% (n = 55), followed by blood group A at 33.6% (n = 37), blood group B at 10.9% (n = 12), and blood group AB at 5.5% (n = 6) (Figure 2). Concerning the RhD factor, Figure 3 indicated that 87.3% (n = 96) of the participants were Rh-positive, whereas 12.7% (n = 14) were Rh-negative.

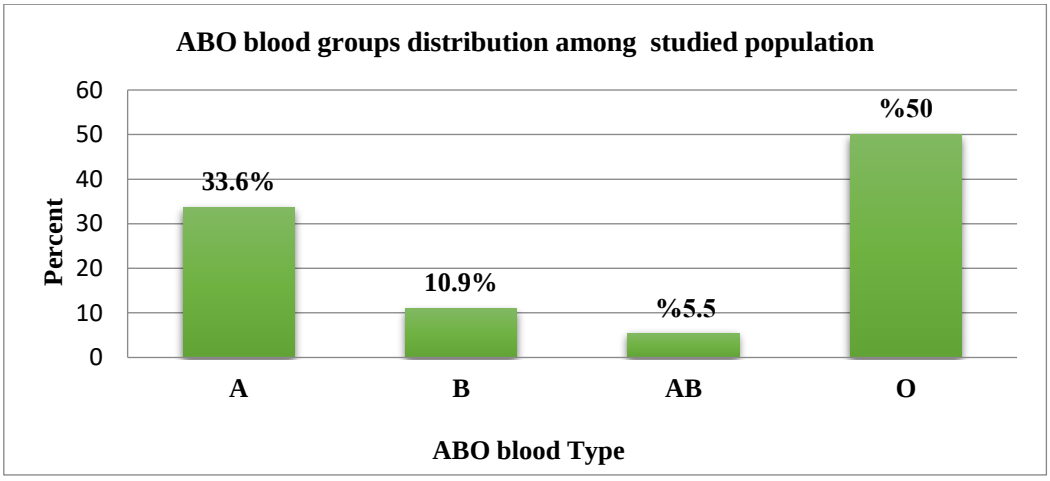

Figure 2. The distribution of ABO blood groups among studied subjects

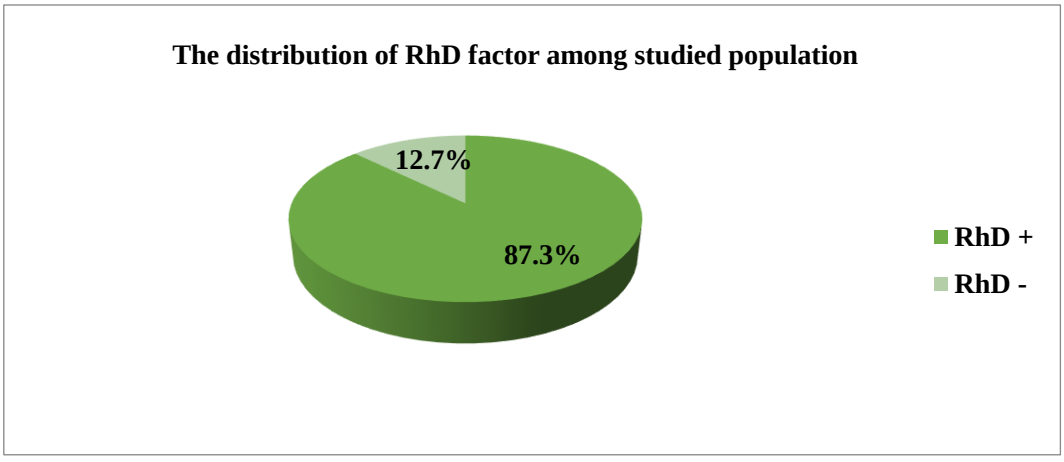

Figure 3. The distribution of RhD blood type among the studied patients

The distribution of ABO and RhD blood groups was observed as follows: O+ > A+ > B+ > O- > AB+ > A- > B- , with respective prevalence rates of 42.72% (n = 47), 30% (n = 33), 9.09% (n = 10), 7.27% (n = 8), 5.45% (n = 6), 3.63% (n = 4), and 1.81% (n = 2) (Figure 4).

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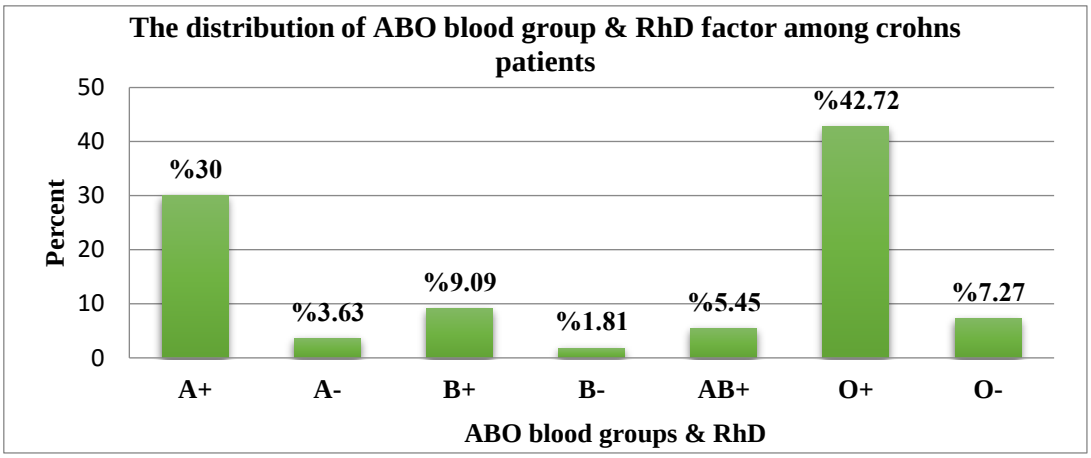

Figure 4. The distribution of ABO & RhD blood types among CD patients

Figure 5 revealed that the prevalence of familial inflammatory bowel disease was 26.4% in a population-based study of 110 patients with Crohn's disease (CD). 17.3% (n = 19) of the index cases had first-degree relatives, and 9.1% (n = 10) of the index cases had second-degree relatives.

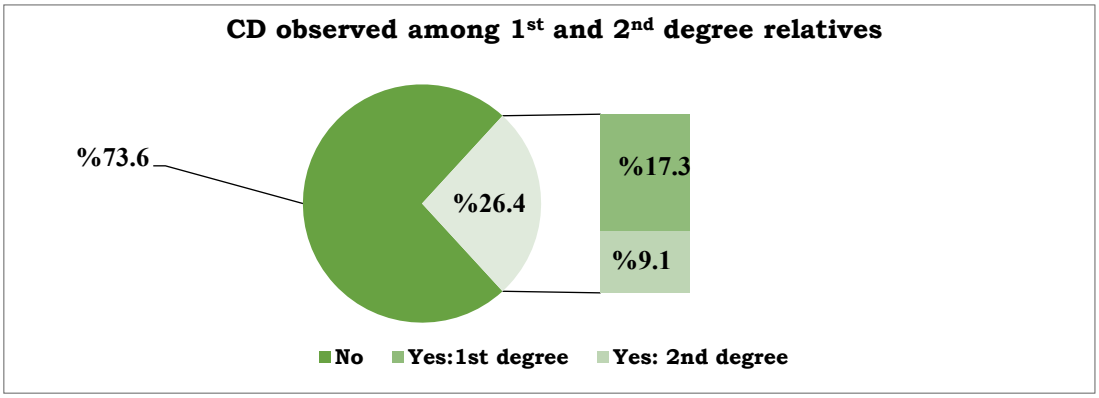

Figure 5. The prevalence of CD observed among first & second -degree relatives

Discussion

CD disease has become increasingly prevalent, with a rise in incidence reported across all age groups. The study included a total of 110 cases ranging from 10 to 70 years. The mean age at the time of study inclusion was 32.57±12.24 years, which aligns with studies conducted in China and Western countries, reporting a mean age of 32.82 years [21]. The initial findings examined the prevalence of CD across different age groups, revealing that the most susceptible were adults aged 20 to 39 years, accounting for 64.5%, followed by middle-aged adults aged 40 to 59 years, at 22.7%, and the least susceptible group being adults over 60 years old. In contrast, a study conducted in India found the highest number of CD cases in the 0–9-year-old age group [22]. Furthermore, findings from an American study indicated that the 10-17 age group was the main contributor to the increasing prevalence of pediatric IBD, including CD [23]. Similarly, in our study, the mean age at diagnosis was 25.92 ± 11.04 years, aligning closely with a study conducted in Saudi Arabia, which reported a mean age at diagnosis of 25 years [24].

Numerous global studies have highlighted an association between blood groups and susceptibility to diseases, including various autoimmune disorders, malignancies, cardiovascular diseases, stomach ulcers, and diabetes [21]. The findings from the present study, which examined the ABO blood groups among CD patients, indicated that the O group was the most commonly affected, with a prevalence rate of 50%, followed by the A group at 33.6%. The B group had a prevalence rate of 10.9%, while the AB group was the least affected, with a rate of 5.45%. These results contrast with previous studies, such as those by Chen et al., which demonstrated that non-O blood groups were significantly associated with a higher risk of CD in the Chinese Han population, as well as findings by Forni et al., which indicated that non-O blood groups are more prone to developing more severe disease behavior [14, 20]. Some studies have explored the potential role of ABO blood groups in the development of IBD. However, a cohort study conducted in Belgium and Italy found no association between CD risk and ABO variables [20].

Regarding the D factor, Figure 3 indicates that 87.3% (n = 96) of the study subjects were Rh positive, while 12.7% (n = 14) were Rh negative. According to many worldwide studies, CD tends to cluster in families. First-degree relatives of people with CD have a higher risk of developing it. In this research, which was subjected to determining the inheritance nature of CD, it was revealed that the non-heritable proportion

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was 73.6%, while there were 19 patients (17.3%) who had a first-degree family history of illness, and 10 (9.1%) were classified as second-degree hereditary (Figure 5). The familial incidence of Crohn's disease in a study conducted in Saudi Arabia revealed that 7% had a first-degree relative with CD, while 1.7% had a second-degree relative with CD [24]. Moreover, a study conducted in India showed that the majority of affected family members were first-degree relatives (3.27% of CD) [22].

Conclusion

Our results confirmed that higher O blood types were associated with an increased risk of developing CD. Additional investigations are warranted to clarify how ABO blood groups influence the pathogenesis and progression of CD. The age groups in this study that were most affected were 20–39 years old.

Conflict of interest

We declare no conflict of interest

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