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Research Article

Increasing Incidence of Crohn's Disease in Epirus, Greece: A 30-Year Prospective Study from a Referral Center

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Abstract

Background: The number of individuals affected by these diseases has been globally increasing, a fact that raises the incidence of morbidity.

Aim: The aim of the study was to investigate in our IBD referral center the incidence and prevalence of IBD and its subtypes (UC, CD, IBD unclassified) in Epirus which is a well-defined geographical area of Greece over a 30-year observation period.

Methodology: The epidemiological study was conducted in the region of Epirus, one of the 13 prefectures of Greece, and in the two neighboring islands of the Ionian Sea, Corfu and Lefkada. The study was conducted in two periods, 1982 - 2002 and 2003 - 2015, and concerned the diagnosis of IBD in patients from the areas mentioned.

Results: The overall incidence of CD was 1,16/100.000 inhabitants (95% C.I. 0,62 - 1,60), 1,41 (95% C.I. 0,75 - 2,15) for male's vs (95% C.I. 0,39 - 1,23) for females on the first period (1982 - 2002) and 2,75/100.000 inhabitants (95% C.I. 1,53 - 3,46), 3,67 (95% C.I. 1,96 - 4,71) for male's vs 1,85 (95% C.I. 0,77 - 2,64) for females of the second period (2003 - 2015). The prevalence of UC/100.000 per age group in both the periods is showing a decrease of the prevalence of UC in older ages during the most recent time period. The decrease appears to male patients over 70 years in regard to female patients. Regarding the age distribution of UC, it appears that during the second period is affecting younger ages in a significantly increasing trend, while a noteworthy decrease after the age of 70 has been documented during the second period of the study.

Conclusion: The results of our study seem not to differ from relevant studies in the past at the same region in Greece. Based on international studies, patients with IBD and particularly CD are expected to increase within the next few years. Consistent and prompt monitoring of the patients starting from an early age will provide them with a better quality of living and will decrease the complications.

Keywords: *Inflammatory Bowel Disease; Crohn's Disease; Ulcerative Colitis; Incidence; Prevalence; Epidemiology*

Abbreviations

IBD: Inflammatory Bowel Disease; CD: Crohn's Disease; UC: ulcerative colitis; IBDU: Inflammatory Bowel Disease-Unclassified.

Introduction

Inflammatory Bowel Disease (IBD) is a chronic idiopathic condition represented by two major types, Crohn's Disease (CD) and ulcerative colitis (UC). Both types can affect not only the colon but also other parts of the human system such as the skin, joints, spinal cord,

liver and other vital organs. Both types usually appear to younger individuals mainly at the age of 15 - 40 years, resulting to physical and psychological issues which affect their everyday lives [1,2].

The number of individuals affected by these diseases has been globally increasing, a fact that raises the incidence of morbidity [3]. On a related research conducted a decade ago, it was stated that 4 million people from around the world are suffering from IBD, while 1,4 million of those cases appear in USA with women being the majority [4].

IBD appears at different frequencies depending on the country of research. The countries affected the most are USA (38 - 229/100.000), Sweden and Great Britain (269/100.000) [5-7]. In the Mediterranean countries UC is estimated to affect 5/100.000 inhabitants of urban areas [8]. In Asia, UC has been increasing especially after 2000, while IBD has been appearing more often to several other countries as well, such as India, Korea, Iran, Lebanon, Thailand etc. [9-11]. It seems that changes regarding nutrition habits such as the consumption of fast food, the reduction of fibers together with the hectic lifestyles and the stress have increased the incidence of the disease [11,12].

In Europe the incidence of the disease is presenting higher in Northern Europe than in the Southern. It also occurs that UC is more common than CD in Europe with the exception of Germany, France and Great Britain [13-15]. According to studies, UC has affected on a more limited basis countries such as Greece, Hungary and Spain [16,17].

A study conducted in a region of Greece has shown that UC is gaining ground comparing to CD, which appears seldom [18]. The annual incidence of IBD for the period 1981 - 1992 was 4/105 residents and for the period 1992 - 1997 was 7,5/105 [13]. In a respective research conducted in northwestern Greece the incidence of IBD was between 5,55/105 to 8,94/105 in the region of Ioannina while to a proximate island area was 2,69/105 and 10,55/105 for the respective periods. The same research showed that the connection between UC and CD is decreased [12,3:1 (1982 - 1991) to 8,01:1 (1992 - 1997)]. In another region while the gap between the two types of the disease remains stable, the levels of the diseases appear significantly lower than in other areas [4,14:1 (1982 - 1991) and 4,75:1 (1992 - 1997), respectively [19].

The aim of the study was to investigate in our IBD referral center the incidence and prevalence of IBD and its subtypes (UC, CD, IBD unclassified) in Epirus which is a well-defined geographical area of Greece over a 30-year observation period.

Material and Methods

The epidemiological study was conducted in the region of Epirus, one of the 13 prefectures of Greece, and in the two neighboring islands of the Ionian Sea, Corfu and Lefkada. The region of Epirus covers a land of 9.203 square kilometers with a population of 336.856 inhabitants according to the census of 2011. Corfu occupies 592 square kilometers and has a population of 104.371 inhabitants, while Lefkada occupies 325 square kilometers and has 25.720 inhabitants. The population of the study concerns natives at the age of 1 - 89 years, living in urban and rural areas, bearing all the cultural characteristics of each area.

The study was conducted in two periods, 1982 - 2002 and 2003 - 2015, and concerned the diagnosis of IBD in patients from the areas mentioned. For the first period of the study, the population (according to the census) in northwestern Greece was 339.728 and for the second period was 336.856.

In the study, all patients examined and diagnosed with IBD (UC or CD) in the University Hospital of Ioannina, the General Hospital "G. Chatzikosta" and the collaborative gastroenterologists of northwestern Greece were recorded. Demographics, place of birth and residence, type of the disease and its location, the total of years since the first diagnosis, morbidity and the incidence of cancer, were also recorded.

Statistical Analysis

Prevalence was calculated to highlight the burden of IBD. Prevalence of IBD was defined as the number of prevalent cases per 100,000 population. Moreover, the incidence of IBD was summarized using incidence rates, defined as the number of cases in a population. The incidence rates per 100,000 population with 95% confidence intervals were estimated. The referral population was calculated using annual estimated numbers derived from the 1991 and 2011 census. Data were divided into 2 censuses: (a) 1982 to 2002, (b) 2003 to 2015. All numbers were calculated for every 10^5 inhabitants per gender, age groups and census. The results were conducted using excel and the statistical program SPSS 25.

Results and Discussion

The results concerning both of the time periods that the study was conducted were initially differentiated in regard to the number of the patients diagnosed with IBD.

During the period 1982 - 2002 the male population of the region was 166.830 (49%) and the female population was 172.898 (51%). On the total, a 0,13% (n = 466) of the population participating in the study was diagnosed with the disease of which a 62% (n = 290) were male patients and a 38% (n = 176) were females. From the total population of the study, a 0,023% (n = 79) was presented with CD, a 0,10% (n = 370) with UC and a 0,005% (n = 17) with IBDU. Male patients presented with higher frequency in both CD (59,4%) and UC (62,6%).

During the period 2003 - 2015 the male population of the study was 165.775 (49%) and the female population was 171.081 (51%). On the total, a 0,001% (n = 373) was diagnosed with the disease, of which a 64% (n = 240) were males and 36% (n = 133) were females. Male patients presented with a higher frequency in both CD (66%) and UC (66%).

Crohn's Disease

On the first period (1982 - 2002) 78 were documented with CD (47 males vs 31 females) and on the second period (2003 - 2015) 111 patients (73 males vs 38 females).

Chart 1 presents the age distribution of the sample for the two study periods. For the period 2003 - 2015, has been observed that from the age of 15 up to 49 years there is a continuous increase of patients with CD. Similar are the results concerning the male patients of the period mentioned.

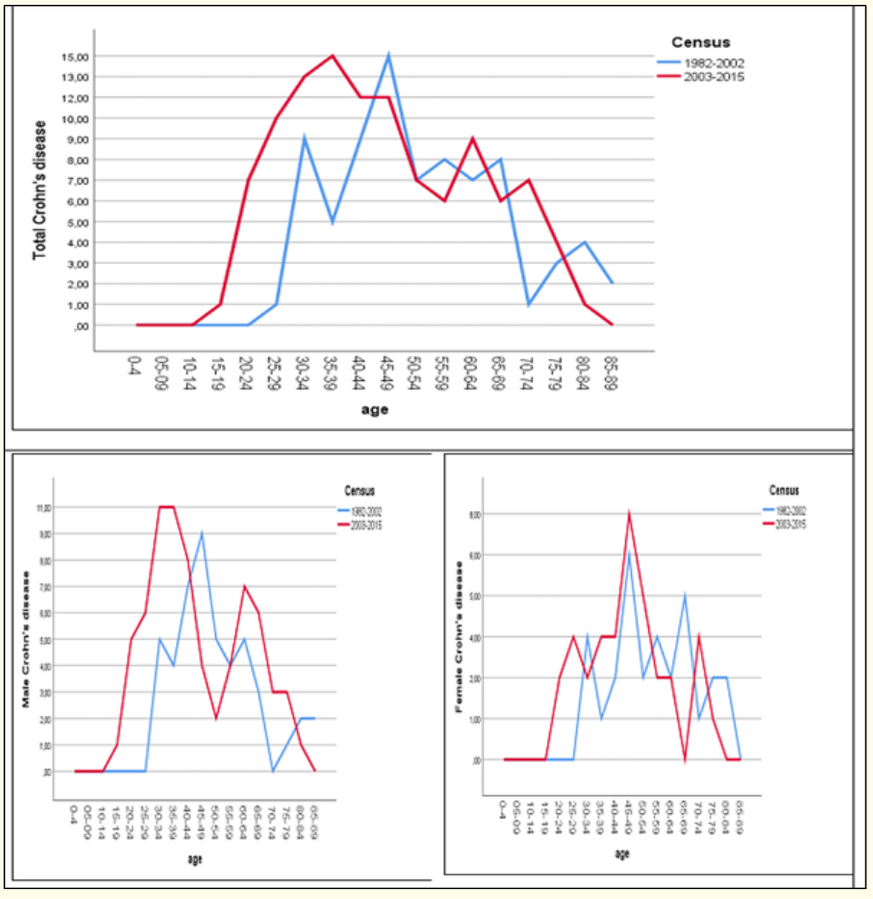

Chart 1: *Age distribution and gender of the sample for the two study periods.*

The prevalence of the patients per 100.000 of population and the relevance according to the census /105, were on the total 23,3% (28,2% males vs 17,9% females) for the first period and 33% (44% males vs 22,2% females) for the second, while the age distribution for both the periods is being presented on chart 2.

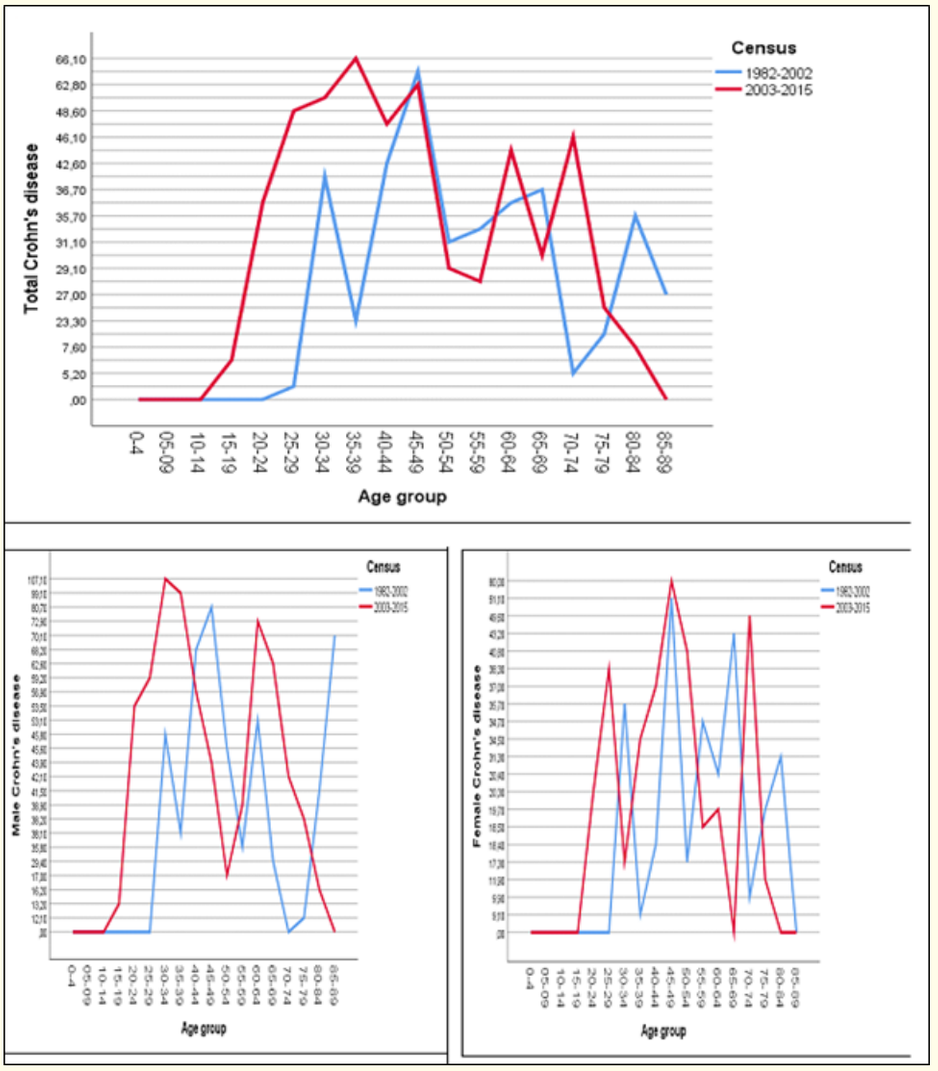

Chart 2: *Prevalence CD. Total per age group/decade and gender.*

The overall incidence of CD was 1,16/100.000 inhabitants (95% C.I. 0,62 - 1,60), 1,41 (95% C.I. 0,75 - 2,15) for male's vs (95% C.I. 0,39 - 1,23) for females on the first period (1982 - 2002) and 2,75/100.000 inhabitants (95% C.I. 1,53 - 3,46), 3,67 (95% C.I. 1,96 - 4,71) for male's vs 1,85 (95% C.I. 0,77 2,64) for females of the second period (2003 - 2015) (Chart 3).

Ulcerative Colitis

The prevalence of UC/100.000 inhabitants for the first period was reported as 108,6 and for the second as 73,6. Male patients were more than the females (137,3 vs 79,8 και 98,9 vs 49,1). The prevalence of UC/100.000 per age group in both the periods is showing a decrease of the prevalence of UC in older ages during the most recent time period (Chart 5). The decrease appears to male patients over 70 years in regard to female patients.

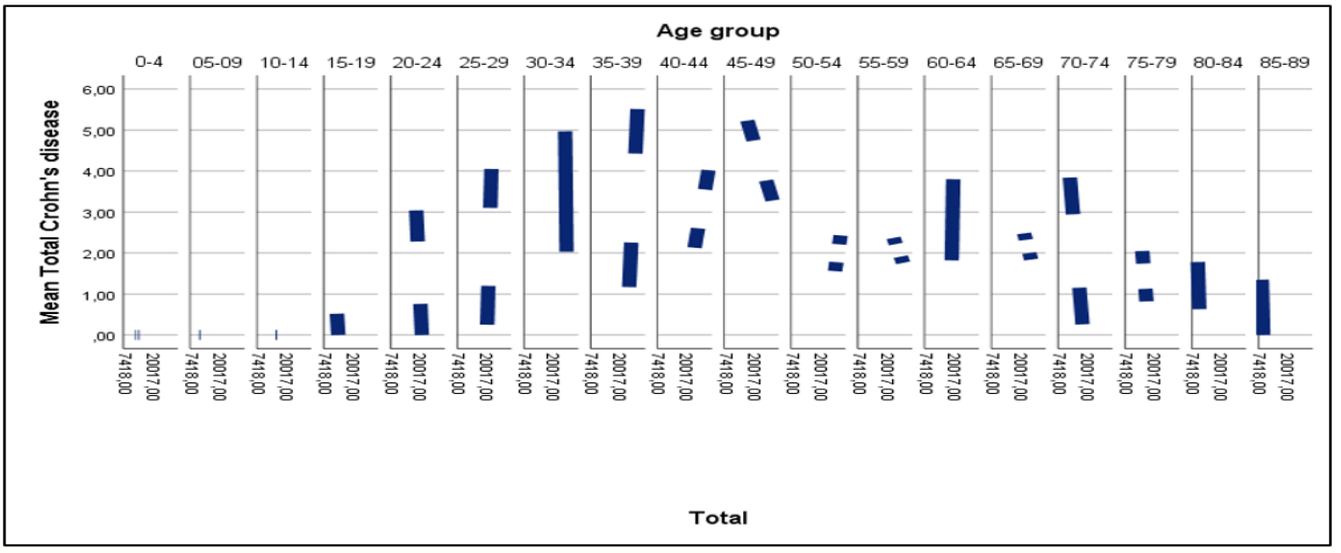

Chart 3: *Incidence of CD. Total by age group compared to population.*

Chart 4: *Total population of UC per age group /decade and gender.*

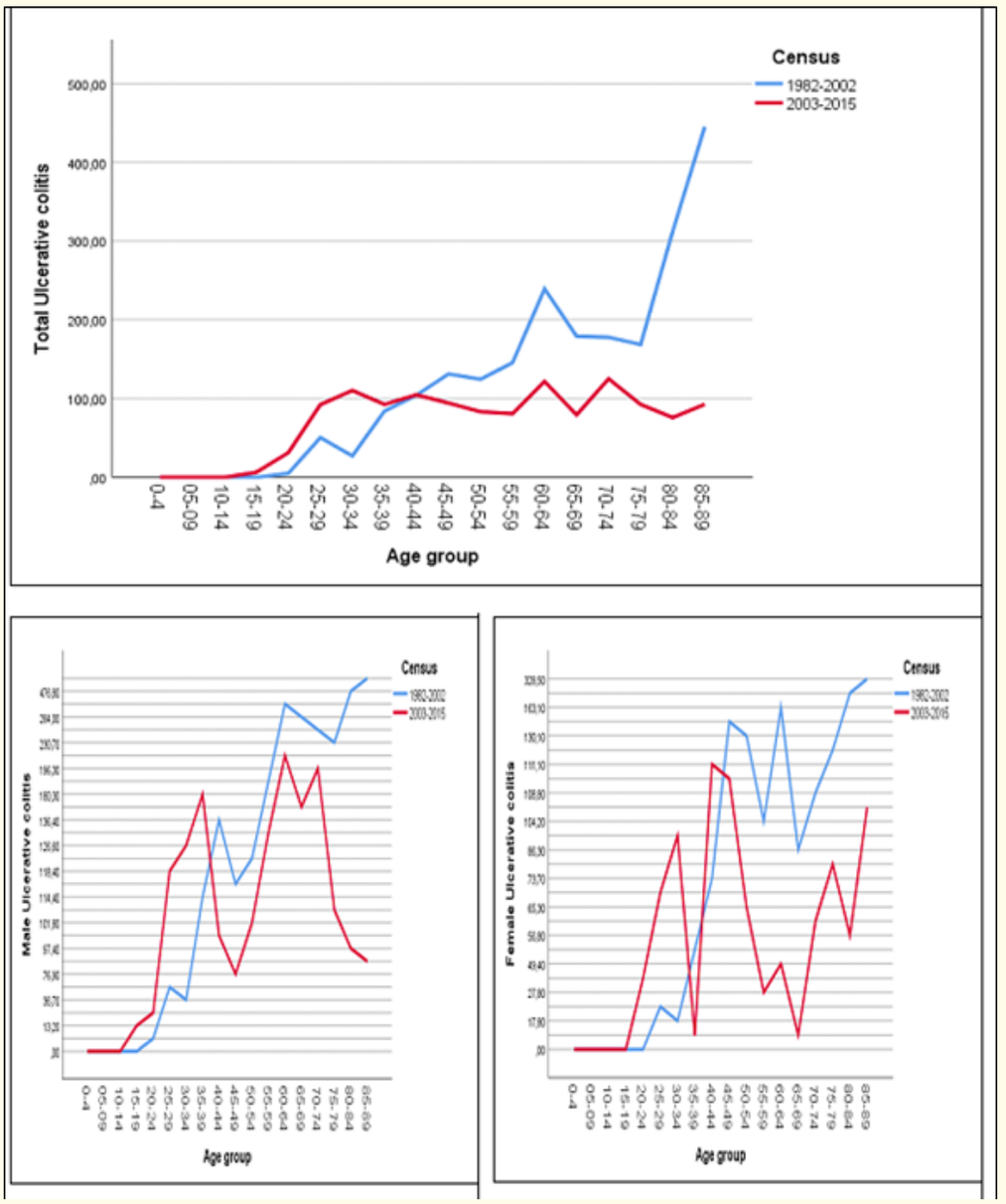

Chart 5: *Prevalence of UC. Total per age group/ decade and gender.*

The total incidence of UC was 5,43/100.000 inhabitants (95% C.I. 3,06 - 9,12) and in specific, 6,86 for men (95% C.I. 3,91 -12,69) vs 3,99 for women (95% C.I. 2,10 - 6,44) during the first period (1982 - 2002) and 6,14/100.000 inhabitants (95% C.I. 4,14 - 7,73), 8,24 for men (95% C.I. 5,20 - 10,66) vs 4,09 for women (95% C.I. 2,38 - 5,77) during the second period (2003 - 2015). Regarding the age distribution of UC, it appears that during the second period is affecting younger ages in a significantly increasing trend, while a noteworthy decrease after the age of 70 has been documented during the second period of the study (Chart 6,7).

Inflammatory Bowel Disease-Unclassified (IBDU)

The total number of patients with IBDU disease between the first and the second period was (n = 17 vs n = 14). The distribution between male and female patients was (n = 9 vs n = 7) during the first period and (n = 3 vs n = 11) during the second period. The prevalence of IBDU cases/100,000 inhabitants for the first period is 5.0 (men 5.4 vs. 4.0 women), while during the second period prevalence shows a small decrease to 4.2 (males 1.8 vs. females 6.4). Respectively, the incidence of IBDU/100,000 inhabitants is 0.25 (95% CI 0.13 - 0.40) in the population, 0.27 (95% CI 0.07 - 0.57) for male patient's vs 0, 20 (95% CI 0.04 - 0.36) for female patients in the first period and 0.35 (95% CI 0.14 - 0.41) for the population, 0.15 (95% CI 0 - 0, 02 - 0.29) for male patients vs. 0.54 (95% CI 0.18 - 1.04) for female patients in the second period (Chart 8).

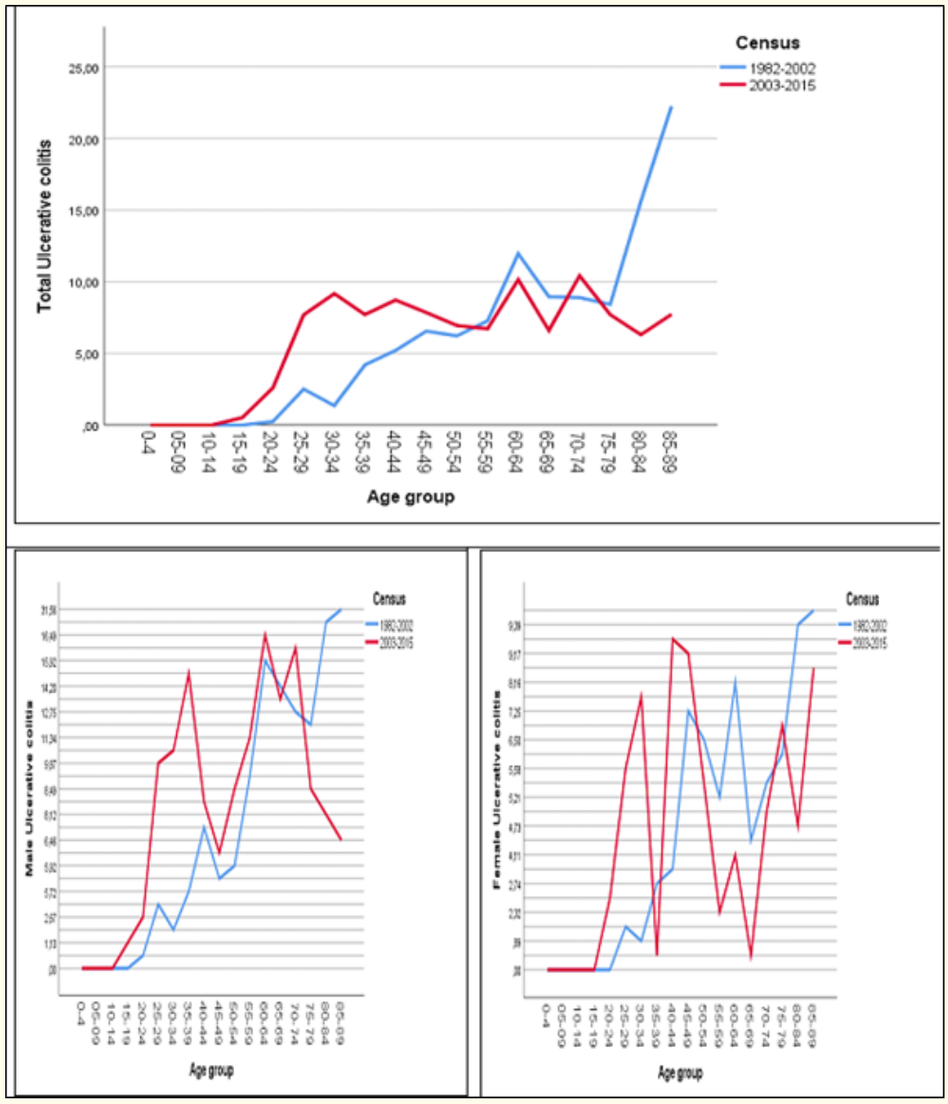

Chart 6: *Incidence of UC. Total population per age/decade and gender.*

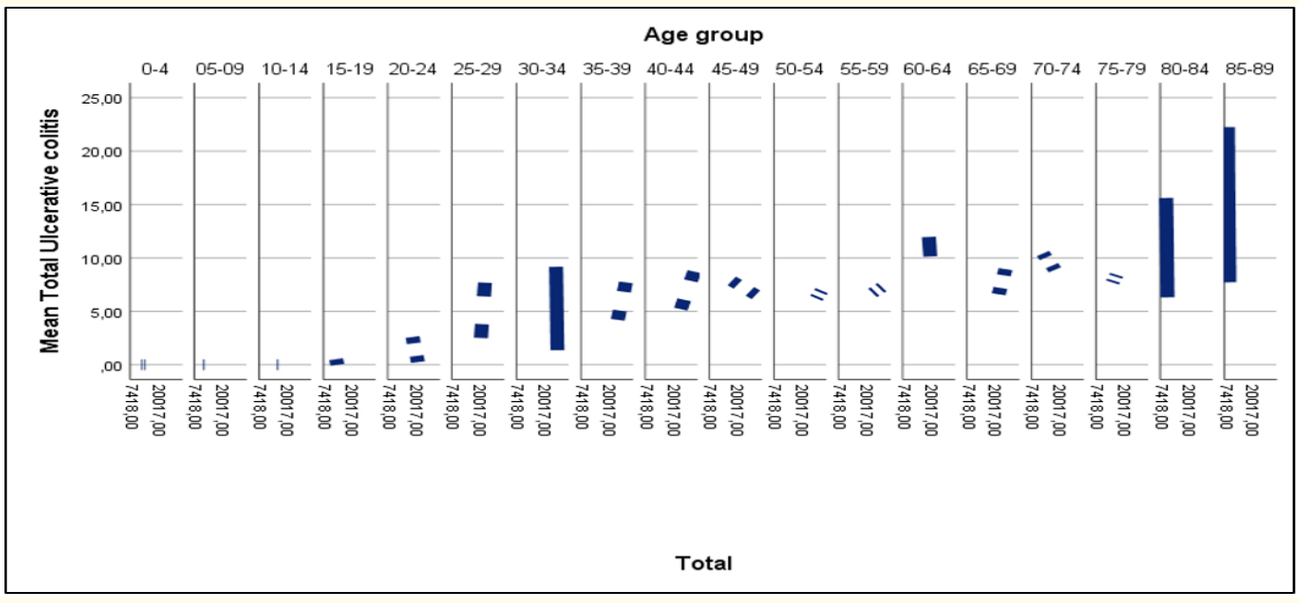

Chart 7: *Total Incidence of UC per age.*

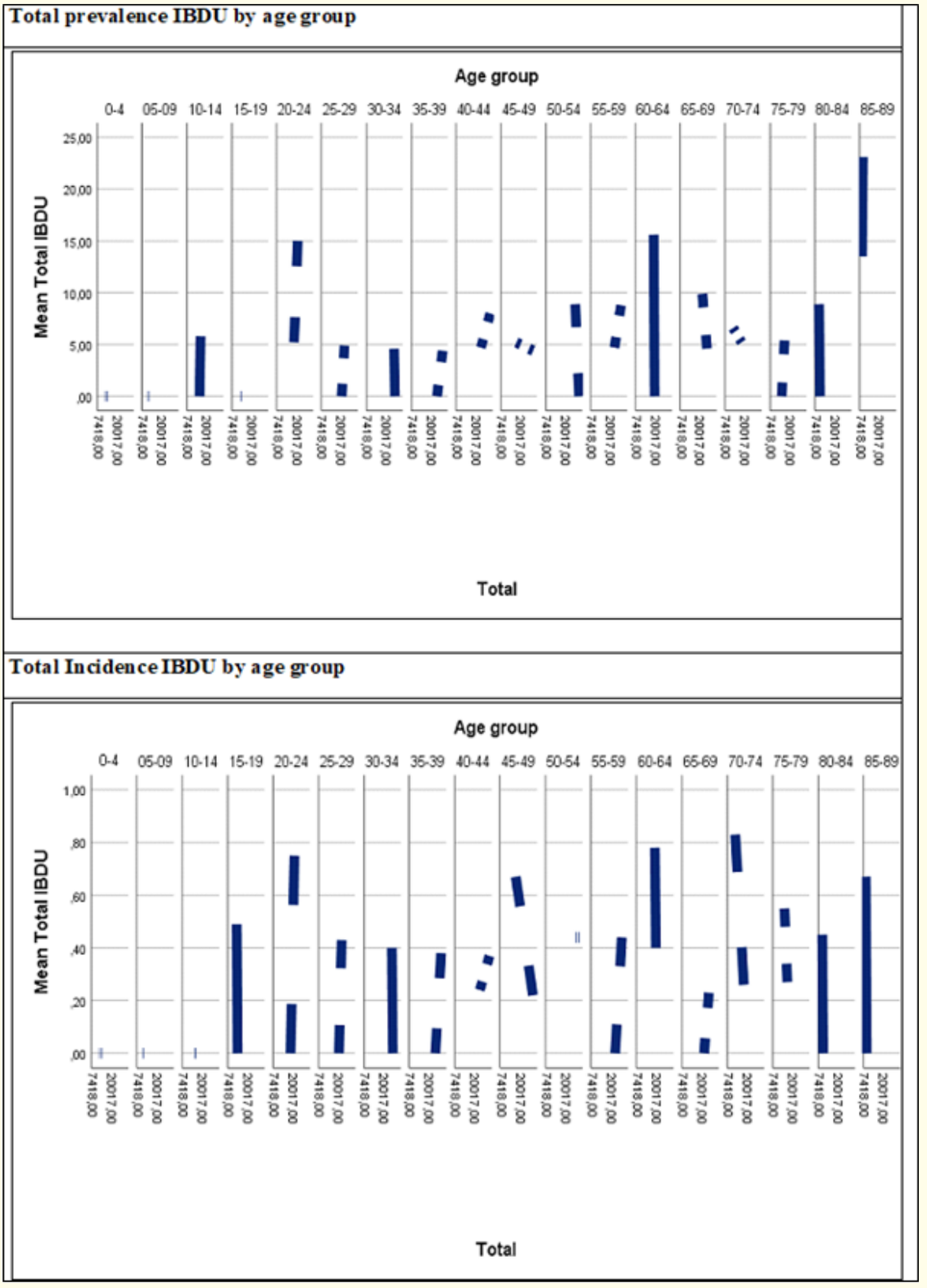

Chart 8: *Prevalence of IBDU per age.*

Discussion

IBD has an increasing tendency globally [22]. However, relative studies in Greece show lower incidence rate in comparison with other countries [14,16,18]. The findings come from an attempt for a systematic record keeping and monitoring patients with IBD in a large re-

gion of SW Greece during two periods of time (1982 - 2002 and 2003 - 2015). This attempt is one of the largest studies in Greece according to the length of time and the documented sample.

In total, although the incidence of IBD has been decreasing, the prevalence has been increasing in the course of time, in particular more for CD than UC. More precisely, the findings in our study showed that the incidence of IBD has been decreasing during the most recent period comparing to the past, while men outnumber women during both periods.

The results of our study seem not to differ from relevant studies in the past at the same region in Greece [19]. In comparison with European studies, seems that the incidence of IBD in NW Greece is lower than in other European countries and in particular it conforms to the low incidence rates in Southern Europe [14,16,18,20-22]. Although the incidence of IBD has been low in countries in Eastern Asia, in recent years CD and UC are on the increase [23-26]. It is worth noting that the increase in IBD has been growing in mobile populations, like immigrants from eastern countries, a fact that possibly proves that western diet and lifestyle are triggering factors of the condition [27].

The incidence of CD is higher in men than women, seem to increase during the two periods and most prominently decreases in both sexes after the age of 65. The prevalence of CD increases significantly during the second period, while age groups 25 - 40 in male and 40 - 50 in female patients have the biggest increase during this period. Studies from around the world and the increasing incidence of IBD [22,26,28] correspond, with the pediatric populations as the only exceptions [29].

The incidence of UC is also lower during the second period, especially for male patients, but the important finding is that it occurs in younger people in comparison to the past. These facts accord with other foreign studies that show the occurrence of the condition in younger ages [3,4].

It's worth mentioning that the decrease in male patients after the age of 60 is vertical, while in female patients It is not and after the age of 70 seems to be on the increase. The prevalence of UC decreases, especially after the age of 70, in comparison with the first period where the increase was significantly high after the age of 70. The findings of our study accord with similar findings from other studies, which show a significant decrease of UC cases in older age especially in men [30,31].

The cases of IBDU are slightly decreased during the second period, the incidence presents with a minor increase and the prevalence presents with a minor decrease. It seems that the diagnostic skills and the scientific training can be the factors to reduce cases of IBDU. Information and awareness of the population may contribute to the direct diagnosis with the best possible diagnostic approach [31,32].

Based on international studies, patients with IBD and particularly CD are expected to increase within the next few years. Consistent and prompt monitoring of the patients starting from an early age will provide them with a better quality of living and will decrease the complications. Informing the population and giving access to specialized clinics will deliver optimal management results of the disease.

Conflicts of Interest

There is no conflict of interest of any of the authors.

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