

ORIGINAL ARTICLE

ARTICOLO ORIGINALE

Prevalence and distribution of Inflammatory Bowel Diseases in a group of immigrant children. Is Inflammatory Bowel Diseases incidence increasing also in children coming from developing countries?

Prevalenza e distribuzione delle Malattie Infiammatorie Croniche Intestinali in un gruppo di bambini immigrati.

Le Malattie Infiammatorie Croniche Intestinali sono in aumento anche nei piccoli provenienti da paesi in via di sviluppo?

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Summary

Aims. To evaluate rate and number of immigrant children affected by Inflammatory Bowel Diseases; to investigate their family conditions and compliance to therapy; to establish the interval between their arrival in Italy, the onset of the clinical features and time until diagnosis.

Patients and Methods. Four immigrant children from a cohort of 134 patients participating in a three-year survey on Inflammatory Bowel Diseases, referred to 21 Italian centres. Their family history was investigated, including the reasons for coming to Italy and their countries of origin.

Results. The 4 children studied represented about 3% of the whole patient population (134) with Inflammatory Bowel Diseases. Time until diagnosis in the 3 cases with Crohn's disease ranged from 12 to 18 months, whereas the one patient with Ulcerative Colitis was diagnosed immediately. Therapeutic compliance was satisfactory.

Discussion. Although Inflammatory Bowel Diseases is not believed to occur in developing countries, it is found also in immigrants from those areas, and the exceptional presentation in these ethnic groups could be related to a different environmental impact rather than a different genetic susceptibility.

Riassunto

Obiettivi. Valutare percentuale e numero di bambini immigrati affetti da Malattie Infiammatorie Croniche Intestinali. Indagare le condizioni familiari e la compliance terapeutica. Stabilire l'intervallo di tempo tra l'arrivo in Italia e l'insorgenza della malattia e l'eventuale ritardo diagnostico.

Pazienti e Metodi. 4 bambini immigrati appartengono ad una casistica triennale di 134 pazienti affetti da Malattie Infiammatorie Croniche Intestinali, afferenti a 21 centri uniformemente distribuiti in Italia. È stata raccolta l'anamnesi familiare. Si è indagato sul motivo della venuta in Italia. È stata annotata la regione di provenienza.

Risultati. I 4 bambini studiati rappresentavano circa il 3% sul totale (134) dei bambini con Malattie Infiammatorie Croniche Intestinali. Il ritardo diagnostico è stato compreso tra 12 e 18 mesi in tutti i 3 casi di malattia di Crohn. È stato assente nell'unico caso di colite ulcerosa. La compliance terapeutica è stata piuttosto buona.

Key words

IBD • Immigrant children • Genetic susceptibility • Environmental factors

Parole chiave

MICI • Bambini immigrati • Suscettibilità genetica • Fattori ambientali

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Discussione. *Le Malattie Infiammatorie Croniche Intestinali, una volta considerate inesistenti nei paesi in via di sviluppo, possono presentarsi anche in soggetti provenienti da queste aree del mondo e la rarità di presentazione nei gruppi etnici che vivono in queste regioni potrebbe essere spiegata con un differente impatto ambientale piuttosto che con una differente suscettibilità genetica.*

Introduction

Inflammatory Bowel Diseases (IBD) in Europe is currently estimated to have a mean incidence of 5.2/100000 new cases per year¹. This rate varies considerably according to age, as IBD is rather uncommon below two years of age (absolutely rare in the first twelve months of life). Their frequency increases sharply among teen-agers and young adults, with a hyperbolic increment in these first decades of life. A second incidence peak occurs between 50 and 70 years of age, regardless of sex.

The pathogenesis of IBD has greatly changed since 1996, when the first locus for susceptibility to Crohn's disease (CD) was identified. It is located on the pericentromeric region of chromosome 16 (16q12) and it is called IBD1. This gene encoded for NOD2 protein and was found to be changed in 20% of CD cases².

This kind of mutation keeps the "lamina propria" monocytes in a continuous state of activation and activates nuclear factor kB (NF-kB) – a key transcriptional factor involved in triggering immune-inflammatory responses³. Moreover, recent reports have shown NOD2 protein to be a protective and defensive factor against intracellular bacteria also in intraepithelial cells. The dysfunction of this protein leads to an impaired innate immunity with an over-expression of the adaptive one⁴⁻⁶.

Subsequently, at least three more genes involved in IBD pathogenesis have been discovered: IBD2 (12q13), IBD3 (6p13), IBD4 (14q11)⁷.

Another important role in the physiopathology of IBD is played by environmental factors, mainly the intestinal "microflora". In fact, increasing importance in triggering the inflammatory response has been recently attributed to changes in the microflora (particularly for CD)^{2,3,8}.

Patients and Methods

Four children (3 M, 1 F) of immigrant parents were selected from a population of 134 patients (60 M, 74 F; age ranging from 6 to 17 years; 82 with CD and 52 with UC) admitted to 21 Italian centres for IBD from 1999 to 2001. The total cohort was the object of a three-year survey investigating this condition.

Three of these patients were affected by CD (2 M, 1 F) and 1 by Ulcerative Colitis. Their family history was carefully investigated, as were the reasons for moving to Italy.

In particular, the countries of origin and the number of

children with only one foreign parent were also recorded.

Of the 21 centres participating in the study 9 were in Northern Italy, 5 in Central Italy and 7 in Southern Italy and the main islands.

Aims

The aims of this study were to:

- evaluate the rate and number of immigrant children with IBD, from the total number of subjects diagnosed in the 21 centres;
- investigate the living conditions of children's families;
- define the interval between their arrival in Italy and the onset of the clinical features;
- assess whether there had been any delay in the diagnosis;
- investigate therapeutic compliance.

Results

The 4 children studied represent about 3% of the total number (134) of children with IBD.

The 3 immigrant children with CD represented 3.6% of the 82 patients who shared the same pathological condition. The one with Ulcerative Colitis (UC) represented 1.92% of the population; as a matter of fact, he was the only immigrant child of the 52 cases with UC reported in our survey (1/52).

Three of the four children were born in Italy from foreign parents, 1 had only one foreign parent.

Two of those with CD were born in Italy, the third one had come to Italy with one of the two parents to join the rest of the family. One of the patients had one foreign parent.

As to the areas of origin of CD patients, they were from Eastern Europe (former Yugoslavia), Sub-Saharan Africa (Nigeria), Middle East (Jordan).

In the patient who was not born in Italy, the onset of clinical features occurred 7 years after his arrival in Italy.

As to CD, the diagnosis was reached after 18 months in 2 cases and 1 year in the third. Compliance to therapy was rather good in 2 of the children.

The patient with UC was born in Italy from Indian parents; the disease manifested itself when the child was 6 years of age. In this case the diagnosis was made quickly; compliance to therapy was also good.

Discussion

Both UC and CD appear to be more common in some industrialized countries such as Scandinavia, the United Kingdom, North America and less common in Central and Southern Europe, Asia and Africa. Although the incidence of IBD among Blacks in Africa is low, data from the USA show similar rates among Afro-American and Caucasian populations⁹. Our results suggest that IBD, which was not believed to occur in developing countries, may be present also in subjects coming from those areas¹⁰ and that its occurrence in those ethnic groups could be related to a different environmental impact rather than to a different genetic susceptibility¹¹. Indeed, several factors such as infectious diseases, use of a diet poor in highly refined sugars and in esterified fatty acids, and prolonged breast feeding may play a protective role against IBD.

Indeed a multivariate analysis showed that the increased incidence of CD well correlated with dietary intake of total fat, n-6 polyunsaturated fatty acids and animal proteins¹².

This protective role may fail if the native lifestyles and eating habits are modified to adapt to "western ones", allowing IBD to prime upon innate predisposing genetic bases¹³.

Indeed a fibre-rich diet has proven to be protective against IBD and colo-rectal neoplasm.

The high incidence of enteral infections is also consid-

ered protective against IBD, as it acts by engaging the immune mucosal system response towards non-self antigens. There is now sound evidence that the tolerance of intestinal immune system is severely hampered in CD^{4,6,8}.

In developing countries such as India, the differential diagnosis needs to be made between the widespread bacillary dysentery, acute amoebic colitis and antibiotic-induced colitis, on the one hand, and the acute presentation of UC or CD with colonic localization, on the other. Chronic or recurrent colitis also needs to be differentiated from tubercular colitis¹⁴. In any case, the improved social and health conditions, the gradual disappearance of infectious diseases and a better survival, are responsible for the current increased prevalence of IBD in these countries¹⁵.

The therapeutic compliance, in our survey resulted to be related to the family's socio-economic status, improving in higher income families.

Therefore, given the increasing awareness of the disease amongst relatives and parents (aside the physician's), compliance to treatment will have to account for the nutritional and pharmacological needs of immigrant children affected by IBD.

Our survey collected a limited number of IBD cases among immigrant children, but in the next few years this number is likely to increase, in parallel with the growing flow of immigrants, as a consequence of the changes in these people's dietary habits.

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