Inflammatory Bowel Disease (IBD) in Childhood: An Emerging Problem

Inflammatory bowel disease (IBD) denotes a group of disorders characterized by chronic intestinal inflammation, the etiology of which is unknown. It includes Crohn’s disease (CD), ulcerative colitis (UC) and indeterminate colitis (IC). UC is primarily a mucosal disease with almost exclusive colonic involvement in contrast to CD which can result in mucosal to transmural inflammation of virtually any part of the gastro-intestinal tract. In a large prospective study from the United Kingdom (UK) and Ireland, CD accounted for 60% and UC for 29% of childhood IBD. The remaining 11% constituted IC, where a clear distinction between CD and UC is not possible(1). Data from pediatric IBD consortium registry from the USA has shown similar figures(2). Traditionally, diarrhea, abdominal pain and weight loss were considered to be the classical triad of CD. Although abdominal pain is still the commonest symptom (72%), and diarrhea and weight loss are presenting symptom in 56% and 58% of children, only 25% of CD children present with this classical triad(1). Other symptoms may include lethargy (25%), anorexia (27%) and poor growth as well as arthropathy and erythema nodosum. Some children may present with perianal lesions. Crohn’s initial description was of an ileitis and traditionally CD has been considered to be mainly a disease involving terminal ileum. How-ever, recent data suggests that 50% of children diagnosed with CD may have gastroduodenal involvement and 20% jejunal involvement. Only 9% have isolated small bowel involvement and 7% isolated colonic disease. Childhood UC, unlike adult onset UC, is more extensive at presentation. 81% of childhood UC have disease extending to the right colon, majority having pancolitis and only 4% have disease limited to the rectum(1).

There are no published internationally agreed, evidence based, clear diagnostic criteria for IBD. To try and address this problem, in 2005 the IBD working group of the European Society of Pediatric Gastroenterology and Nutrition (ESPGHAN), published “The Porto Criteria” which details a consensus based diagnostic criteria for the diagnosis of childhood IBD(3). It proposes that all children suspected of having IBD should undergo an upper and lower gastrointestinal endoscopy with multiple biopsies. Unless there is a clear cut diagnosis of UC, they should also undergo a barium meal and follow through to visualise the small bowel. This should help to bring uniformity in defining newly diagnosed IBD cases and enable better comparison of the data from different studies from various parts of the world. A prospective anonymised European database has also been established by the ESPGHAN Working Group on IBD with the aim of facilitating future epidemiological studies.

Incidence of IBD in adults may vary significantly from geographical region to region, the highest rates being reported in the Scandinavian countries and Scotland followed by England and Southern Europe(4). The first national prospective survey of childhood IBD from the British Isles(5) documented an incidence of 5.2/100,000 children aged less than 16 years per year. Several other recent studies have reported incidence of childhood IBD from various other parts of Europe and USA including Sweden(6), and Wisconsin, USA(7). Direct comparison of results of these studies is difficult due to difference in study design, population size, age groups and time periods.

However, it can be stated that IBD is now relatively common in most industrialized countries and childhood IBD accounts for nearly 30% of total cases. There appears to have been an increase in the incidence, mainly of Crohn’s disease in most industrialized countries over the last few decades. The reason is not clear; though it could partly be due to increased diagnostic accuracy due to advent of flexible endoscopy, improved technology and increased awareness. A number of environmental factors such as hygiene, diet, breast feeding,
smoking, oral contraceptive pill and infectious agents such as measles, mumps, Epstein-Barr virus, and Mycobacterium para tuberculosis have also been explored(8). Smoking appears to predispose to CD but is protective against UC(8). The increase in childhood and adolescent IBD in recent years in fact has paralleled the overall population trends(9). There is no convincing evidence that age at development of IBD is decreasing(10). IBD can manifest at any age but is rare in infancy. Only 1% of all childhood IBD patients are diagnosed before 1 year of age(2). The incidence increases steadily during childhood and adolescence, peaking at about 14 years of age. There is a later peak in adulthood in the sixth decade. Unlike in adults, pediatric onset CD has clear male preponderance. In the UK study, 62% of pediatric CD in a cohort of 379 children were males(1). Armitage, *et al.*(11) observed an association of CD with affluence. It has been suggested that this may be due to low level/delayed exposure to common childhood infectious agents resulting in altered immune response in genetically susceptible hosts - the so called “hygiene hypothesis”(12).

Extensive research has been undertaken in genetics of IBD. Mutations in NOD2/CARD 15 gene significantly increase the risk of Crohn’s disease and this is particularly associated with ileal location and earlier disease onset(13). These findings underscore the importance of host-bacterial interactions in the pathogenesis of IBD, since these genes are involved in mediation of host resistance to bacterial pathogens.

The incidence of IBD in developing countries is postulated as being low but data limited. Infective colitis are said to be much more common. Mehta, *et al.*(14) from India reported that 5% of children admitted for colonic disorders were diagnosed as UC. Incidence of IBD in South Asian population resident in western countries appear to be higher than that in native population both in children and adults. Epidemiological studies from Leicestershire in the UK, where a high proportion of residents are immigrants from southern Asia, mostly from India and Pakistan, has shown that mean annual incidence of UC in people of southern Asian origin was significantly higher at 13.7/10^5 compared to 6.1/10^5 in native Europeans. Among the south Asians, incidence of UC was high in Hindus and Sikhs where as Muslims showed an incidence similar to that of Europeans(15). In contrast to UC, incidence of CD in Hindus was significantly lower than in Europeans. The mean annual incidences for CD during 1980s were 4.7/10^5 in Europeans, 2.4/10^5 in Hindus, 3.4/10^5 in Sikhs and 5.4/10^5 in Muslims(16). A recent prospective study on 51,910 adults from the Punjab, India(17) suggested that the prevalence there may be similar to that in the UK. After history taking, 147 were suspected of having UC and were endoscoped and biopsied following which 23 were diagnosed as UC. This gave a prevalence rate of 44.3/100,000 (95% CI 29.4-66.6). The exercise was repeated a year later and gave an incidence rate of 6.02/100,000 (95% CI 1.2 -17.6). This figure is almost the same as the incidence rate of 6.1/100,000 published by Probert, *et al.*(15) for Europeans in Leicester, UK.

Recent data from British Isles have shown that significantly greater proportion of children of Asian origin feature among under-5 with IBD (25% vs. 6%) with a relative risk of 3.9(1). The reason for this phenomenon remains unclear but taken together with recent studies including that by Sood, *et al.*(16) suggests that IBD among Asians may not be as uncommon as previously thought. Further studies using agreed criterion for investigation and diagnosis are needed. Etiology of this emerging disease complex remains unknown. Studies examining environmental and other factors that differentiate between children born and growing up in Asia and children of immigrant Asian parents from similar genetic background but growing up in industrialized countries may provide invaluable clues and allow more focused investigation towards possible genetic, environmental and other risk factors. Multinational and multi centre collaboration is essential to successfully undertake these studies.

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