The Epidemiology, Phenotype and Disease Course of Australian Children with Inflammatory Bowel Disease.

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Abbreviations

ACT  Australian Capital Territory
ANOVA  Analysis of variance
APAI BD  Australian Paediatric and Adolescent Inflammatory Bowel Disease database
ASCA  Anti-Saccharomyces cerevisiae
ASA  Aminosalicylates
BMI  Body mass index
CARD15  Caspase recruitment domain-containing protein 15
CD  Crohn’s disease
CI  Confidence interval
CRP  C-reactive protein
EIM  Extra-intestinal manifestation
ESR  Erythrocyte sedimentation rate
GIT  Gastrointestinal tract
Hb  Haemoglobin
HR  Hazards ratio
Ht  Height
IBD  Inflammatory bowel disease
IBD1  Inflammatory bowel disease protein 1
IBDU  Inflammatory bowel disease unclassified
IC  Indeterminate colitis
IgA  Immunoglobulin A
IgG  Immunoglobulin G
IQR  Interquartile range
N  Number of children
NOD2  Nucleotide-binding oligomerization domain-containing protein 2
NSW  New South Wales
NT  Northern Territory
OFD  Orofacial Crohn’s disease
OR  Odds ratio
p-ANCA  Perinuclear anti-nuclear cytoplasmic antibody
PCDAI  Paediatric Crohn’s disease activity index
Plts  Platelets
PSC  Primary Sclerosing Cholangitis
PUCAI  Paediatric ulcerative colitis activity index
QLD    Queensland
SA      South Australia
SMR    Standardised mortality ratio
TAS    Tasmania
UC     Ulcerative colitis
UK     United Kingdom
USA    United States of America
VIC    Victoria
WA     Western Australia
WCC    White cell count
Wks    Weeks
Wt     Weight
Yrs    Years
Abstract

Inflammatory bowel disease (IBD) is the term for a group of disorders of the gastrointestinal tract, encompassing Crohn’s disease (CD), ulcerative colitis (UC) and inflammatory bowel disease unclassified (IBDU). The aims of this study were to review the disease phenotype at diagnosis in children with IBD, investigate any significant associations, determine the incidence in South Australia and to assess the disease course.

Methodology: Phenotypic features at diagnosis of children collected into the Australian Paediatric and Adolescent IBD database (APAIBD) and follow-up details of South Australian children were analysed. Incidence of IBD in South Australia was calculated. Statistical testing included the independent t-tests/ANOVA (parametric), Mann-Whitney/Kruskal-Wallis testing (non-parametric), chi-square analysis, linear and logistic regression, Kaplan-Meier survival, Cox Proportional Hazards, negative binomial regression and linear mixed effects model. P<0.05 was considered to be statistically significant.

Results: There were 2101 children diagnosed with IBD during the period 1996-June, 2010. The majority had CD (1247; 59.4%), followed by UC (631; 30%) and IBDU (223; 10.6%). Overall, there was a male predominance (56.4%), which was significantly greater in CD compared to the background Australian paediatric population (58.6% vs 51.3%; p<0.05). The majority of children with CD presented with ileocolonic disease (57%; 662), upper gastrointestinal inflammation (78.9%; 816) and inflammatory behaviour (92.6%; 1123). Orofacial CD was present at diagnosis in 8.9% (107/1207) and perianal lesions in 46% (545/1184) of children. There was a significant association between orofacial CD and anal tags (p<0.0001), anal fissures (p<0.0001), oesophageal inflammation (p=0.0001), ocular (p=0.0016) and dermatological manifestations (p=0.001). Most children with UC presented with extensive colitis (69.6%; 421/605). Children with CD presented with a lower weight, height and BMI z-scores compared to UC. The incidence of IBD, CD and UC in South Australian children aged less than 16 years was 6.43, 3.62 and 2.31 per 100,000 person years respectively during 1996-2009.

The majority of children were treated with systemic corticosteroids (85% CD; 70% UC) with a clinical remission rate of at least 70% at 6 weeks. Half of these children had a subsequent clinical flare-up within the first year. Compared to CD, a greater proportion of children with UC developed mucosal healing within 5 years (p=0.0037). The risk of developing intestinal strictures or fistulae was 15% at 5 years in CD. Mean duration of systemic corticosteroid use
was 69.3 and 59.7 days per year for CD and UC, respectively. The mean duration of hospitalisation was 5.29 days per year for CD and 6.07 days per year for UC. The rates of intra-abdominal surgery were 16% in CD and 13% in UC within the first 5 years. Weight and BMI parameters improved within the first year following diagnosis in both CD and UC, although the low height z-scores in CD did not improve, despite medical therapy. Two children with CD died as a result of sepsis.

Conclusion: Paediatric IBD is a heterogeneous disease, which impacts upon a child’s health. Despite attaining remission, children are at risk of clinical recurrence, changes in extent and behaviour, side-effects from systemic corticosteroids, surgery and poor growth. Thus, there is a need for improved management to avoid these complications.
Declaration Statement

I certify that this work contains no material which has been accepted for the award of any other degree or diploma in any university or other tertiary institution and, to the best of my knowledge and belief, contains no material previously published or written by another person, except where due reference has been made in the text. In addition, I certify that no part of this work will, in the future, be used in a submission for any other degree or diploma in any university or other tertiary institution without the prior approval of the University of Adelaide and where applicable, any partner institution responsible for the joint award of this degree.

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Dr Rammy Abu-Assi,
1st of April, 2014.
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