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

Dr Rammy Abu-Assi

Discipline/School: Paediatrics

University of Adelaide

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Abbreviations

ACT	Australian Capital Territory
ANOVA	Analysis of variance
APAIBD	Australian Paediatric and Adolescent Inflammatory Bowel Disease database
ASCA	Anti-*Saccharomyces cerevisisae*
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,
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