Journal of Crohn's and Colitis (2013) 7, 542–550

Available online at www.sciencedirect.com

SciVerse ScienceDirect

Maternal inflammatory bowel disease has short and long-term effects on the health of their offspring: A multicenter study in Israel

Iris Dotan [a,i,*], Arik Alper [b,i], Daniel Rachmilewitz [c,i], Eran Israeli [d], Shmuel Odes [e], Irit Chermesh [f], Timna Naftali [g,i], Gerald Fraser [h,i], Ariella Bar-Gil Shitrit [c], Vardit Peles [c], Shimon Reif [b,i]

[a] *IBD Center, Department of Gastroenterology, Tel Aviv Sourasky Medical Center, Tel Aviv, Israel*
[b] *Pediatric Gastroenterology Unit of the Department of Pediatrics, Dana Children's Hospital, Tel Aviv Sourasky Medical Center, Tel Aviv, Israel*
[c] *Department of Gastroenterology and Division of Medicine, Shaare Zedek Medical Center, Jerusalem, Israel*
[d] *IBD Center, Department of Gastroenterology, Hadassah Medical Center—Hebrew University, Jerusalem, Israel*
[e] *IBD Unit, Department of Gastroenterology and Hepatology, Soroka University Hospital, Faculty of Health Sciences, Ben Gurion University of the Negev, Beer Sheva, Israel*
[f] *Rambam Medical Center, Haifa University, Haifa, Israel*
[g] *Department of Gastroenterology, Meir Medical Center, Kfar Saba, Israel*
[h] *IBD Unit, Department of Gastroenterology and Liver Diseases, Rabin Medical Center, Petah Tikva, Israel*
[i] *Sackler Faculty of Medicine, Tel Aviv University, Tel Aviv, Israel*

Received 1 March 2012; received in revised form 21 August 2012; accepted 22 August 2012

KEYWORDS
Inflammatory bowel disease;
Pregnancy outcomes;
Long-term effects

Abstract

Background: There are concerns about the effect of inflammatory bowel diseases (IBD) on fertility, pregnancy and pregnancy outcomes, but no long-term data on the health of offspring born to IBD mothers. The aims were to assess the short- and long-term effects of maternal IBD on the morbidity and development of their offspring.
Methods: Female IBD patients and controls completed questionnaires on their pregnancy outcome, and their offspring's short- and long-term health and development.
Results: IBD and control mothers (159 and 175, respectively) were recruited. Medical data of 412 IBD and 417 control offspring were recorded. IBD mothers had significantly more singleton pregnancies, their offspring's birth weight was significantly lower, and they breastfed significantly

* Corresponding author at: IBD Center, Department of Gastroenterology and Liver Diseases, Tel Aviv Sourasky Medical Center, 6 Weizmann Street, Tel Aviv 64239, Israel. Tel.: +972 3 6947305; fax: +972 3 6974622.
E-mail address: irisd@tasmc.health.gov.il (I. Dotan).

1873-9946/$ - see front matter
http://dx.doi.org/10.1016/j.crohns.2012.08.012

less compared to controls (P=0.028, 0.007, and <0.0001, respectively). There were significantly more congenital anomalies (mainly limb deformities) among the IBD offspring (P<0.035). Offspring born post-maternal IBD diagnosis, compared to pre-diagnosis, tended to have more neurodevelopmental problems (e.g., gross motor delay, P=0.03). IBD was significantly more prevalent in the offspring of IBD mothers, while allergies and atopic dermatitis were more frequent in offspring of control mothers. More offspring of IBD mothers taking medications during pregnancy were born preterm and had lower birth weights compared to offspring of IBD mothers not taking medications during pregnancy. Children of mothers taking steroids had the lowest birth weights, compared to those of IBD mothers taking 5ASAs or immunomodulators.

Conclusions: Maternal IBD affects pregnancy and the offspring's immediate and long-term morbidity, specifically, congenital anomalies and neurodevelopmental problems.

1. Introduction

Inflammatory bowel diseases (IBD) are chronic intestinal disorders usually diagnosed during the second and third decades of life. Consequently, female IBD patients may develop active disease and require treatment at the time of conception, pregnancy or delivery.[1] Concerns that their children carry an increased risk for inheriting IBD and effects on fertility and pregnancy can lead patients to voluntarily remain childless.[2] Large-scale studies have assessed the effects of IBD on pregnancy and its immediate outcomes.[3–6] Active IBD was reported to have a negative effect on pregnancy by increasing the risk of spontaneous abortions, preterm deliveries, and small-for-gestational-age babies. Some authors have suggested that more chromosomal defects may occur in IBD patients, although the role of disease activity versus that of the medication taken was not clarified.[3–6] The effects of IBD on the long-term outcomes of pregnancy have not yet been determined. The current study aimed to assess the effect of maternal IBD during pregnancy on the short and long-term outcomes of their offspring in the Israeli population.

2. Methods

2.1. Study population

This multicenter prospective study in Israel was performed in 2004–2009. It included patients from 7 major IBD centers representing all parts of Israel. It was conducted with the approval of the local ethics committees of all participating IBD centers, together representing the nationwide population. Any female IBD patient who had given birth was eligible for study entry and was consecutively offered to fill in questionnaires during clinic visit. The control group comprised of non-IBD females who had given birth, and in each Medical Center representing different parts of Israel, they were recruited from hospital personnel (medical, paramedical and administrative) and their relatives, contacts and subjects from their domestic area. They described themselves as being in good health and none had been using any medications chronically during pregnancy.

2.2. The questionnaires

Each subject had a medical interview performed by a physician and filled in a detailed questionnaire containing selected demographic and clinical items. Subjects with IBD also provided clinical data on their disease (Crohn's disease, ulcerative colitis), including time of diagnosis and the use of IBD medication prior to or during pregnancy. Ethnicity was determined by subdividing the participants into the two common ethnic groups among Israeli Jews (Ashkenazi and Sephardic). A separate questionnaire was filled in for each child, and it contained detailed information on the child's birth and neonatal history, including length of pregnancy (preterm delivery was defined as gestational week <37), method of delivery, birth weight, congenital anomalies, developmental milestones according to the Denver Developmental Score,[7] learning performance and illnesses during the first few years of life.

2.3. Statistics

All the data from the questionnaires were entered in a dedicated database constructed using SPSS software. As some participants only partially completed the questionnaire, the data in the tables are presented as the percentage of participants out of the ones completing the specific section. Items that had less than 5% missing data were imputed according to the hot-deck method. Association between categorical variables was examined using the chi-square test or Fisher's exact test. A two-sample t-test was applied for determining the association between binary and continuous variables. Analysis of variance (ANOVA) was performed using a one-way ANOVA or the non-parametric test of Kruskal–Wallis. The RYAN–Einot–Gabriel–Welsch multiple-range test was employed to determine significant differences between pairs of groups. A P<0.05 was considered statistically significant. Data are presented as mean ± SD. In specific sections, the median and range are presented. All statistical analyses were performed using SAS for Windows 9.1.3.