INFLAMMATORY BOWEL DISEASE AND PREGNANCY:
A prospective European case-control study

BACKGROUND

Inflammatory Bowel Disease (IBD) commonly affects women during reproductive years and a quarter of patients conceive after the diagnosis of their disease.
The patients are concerned about pregnancy and ask their physicians mainly these questions: what are the effects of IBD on pregnancy? What are the effects of pregnancy on IBD? What treatment is appropriate and safe for the developing fetus during pregnancy?
Many studies have described the outcome of pregnancy in IBD patients (1-8, 22-25), the influence of pregnancy on the course of the diseases (1, 4, 9-11, 27) and the safety of drugs used to treat these diseases (5, 12-21). In some studies it is reported (18-19) an increased risk of pre-term delivery in patients with IBD even in pre-diagnosis pregnancies, in patients with a subsequent diagnosis of CD and of UC, while in post-diagnosis pregnancies the risk is increased only in CD patients.
Moreover it is highlighted an increased frequency of low birth weight babies in most (1, 3, 4, 6), although not all studies (26). In large studies congenital abnormalities in infants born to women with IBD are not increased compared to general population (4, 5, 21, and 26). The spontaneous abortion or stillbirth rate in CD and UC seem to be related to disease activity during the pregnancy (1, 2, 4, and 26). In most patients the pregnancy has little effects on disease activity (4, 26, and 27) and, if a relapse does occur, predilection for the first trimester is reported.

Of these studies, mainly retrospective, however, many are merely descriptive, while few are controlled. Moreover, the available studies are difficult to compare, because they differ widely in methods used, data on some issues is insufficient because of small number.
In particular for treatment advice to the patients is based not only on evidence of IBD patients, but even extrapolated from different diseases.
In conclusion the literature data is still controversial.

Therefore a large multicenter prospective study is a perfect opportunity to evaluate all the parameters about IBD and pregnancy.

AIM OF THE STUDY

To evaluate the pregnancy outcome and the disease course in women with IBD and to evaluate the influence of treatment on the outcome of pregnancy

PATIENTS AND METHODS

This is a multicenter, prospective and case-control study.

We will enroll pregnant women with CD and UC that will be interviewed, during pregnancy and in the post-partum period (6 months), at least once every three months.
The interview will be made by a physician of the referral center using a standard questionnaire about outcome of pregnancy (abortions, pre-term delivery, live births, birth-weight, congenital abnormalities, mode of delivery). The questionnaire also includes a section about course and treatment of the disease at conception, during pregnancy and in post-partum period. ATTACHMENT 1.
For control group we will collect, prospectively, one pregnancy, in general population, for each patient's pregnancy. The control subjects will be matched for maternal age at conception ($\pm$ 2.5 years) and gravidity. The matched control women will be selected in Obstetric and Gynecology Department of each participating center, followed-up during the gestation period and interviewed at least once every three months. ATTACHMENT 2

A particular and important point concerns the effects of the pregnancy on the course of IBD. To investigate the influence of the pregnancy on IBD it is mandatory to compare the course of the disease in pregnant and

in non-pregnant IBD patients ("control patients group"). Non-pregnant control patients will be matched to the pregnant patients with CD and UC by age, type of disease, extent of the disease, duration and severity of the disease.
The non-pregnant control patients will be followed-up during the study period (for 15 months) and interviewed every three months. ATTACHMENT 3.

Because it could be difficult to find a non-pregnant IBD patient that matches the index case in each center, we suggest to ask other participating centers (within each Country) to find one.

We plan to enroll about 500 pregnant patients, about 1000 control pregnancies in general population and about 500 non-pregnant IBD control patients. The duration of the study will depend on the number of the participating centers. The study will be closed 15 months after the inclusion of the last pregnant patient.

PUBLICATION POLICY

The results of this study will be presented at major Gastroenterology meetings.
The final version of the paper (after approval of all participating centers) will be published under a collective name (European Crohn's Colitis Organization). The individual centers and the names of all participating investigators will be published in a list accompanying the manuscript.

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