ORIGINAL PAPER

THE IMPACT OF RHEUMATIC AND GASTROINTESTINAL AUTOIMMUNE DISEASES ON PREGNANCY

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ABSTRACT

Pregnancy promotes immune and endocrine adjustments in order to facilitate nidation, placentation and fetal development, inducing an immunological reset and triggering a potential autoimmune disease. The aim of the study is to analyze the impact of an underlying rheumatic or gastrointestinal autoimmune disease on pregnancy. The study is retrospective, unicentric, and included a group of 70 patients. The awareness regarding reproduction in women with rheumatic diseases made pregnancies possible and with fewer complications along the way, imputing interdisciplinary management and pre-conceptional counselling. Pregnancy complications as pregnancy loss, cesarean delivery, preeclampsia, intrauterine growth restriction, preterm birth are more often among pregnant women with autoimmune diseases, but severe complications like perinatal deaths and structural malformation are rare. The take home message of these research is that pregnancy in woman with autoimmune diseases should be multidisciplinary monitored due to possible placental transfer of maternal autoantibodies, the possible effects of maternal medications on the fetus and the newborn.

KEYWORDS: *pregnancy, autoimmune disease, fetal complications, treatment*

INTRODUCTION

Autoimmune diseases are heterogenous group of diseases that are based on extensive chronic systemic inflammation and autoantibody production and it is known to be correlated with reproduction problems in both genders. These inflammatory systemic diseases are frequently diagnosed in the 20 or the 30 decades of life and after that they impact the entire life span, but are more prevalent in childbearing age women. Pregnancy promotes immune and endocrine adjustments in order to facilitate nidation, placentation and fetal development, inducing an immunological reset and triggering a potential autoimmune disease [1], [2]. This physiological pathway of inflammation during pregnancy plays an important role in obstetrical and neonatal outcomes. As inflammation is the key in autoimmune diseases, pregnancy will be challenging at these patients.

Unfortunately, until recent times, women with underlying autoimmune diseases, had been discouraged regularly from pregnancy due to condition flare or unknown obstetrical and fetal outcomes. During pregnancy or postpartum, conditions as such, if not controlled properly, can lead to activity flare, thromboembolic events, hypertension, renal vasculitis, etc. [3]–[6]. Fetal outcomes in pregnant women with underlying autoimmune diseases are represented by preterm delivery, fetal loss, cesarean delivery, preeclampsia and intrauterine growth restriction [3], [5]–[7].

Even though the course of an autoimmune disease during pregnancy differs from one condition to another, there is a consensus regarding the fact that the a minimally active disease or a sustained remission before and during pregnancy and a controlled preconception can guarantee a successful maternal and fetal outcome [8], [9]. Modern day medicine succeeded to present complex treatment options, to address contraception and conception planning for a better and safer pregnancy outcome.

MATERIALS AND METHOD

The methodological characteristics of the study on the basis of which the research design was established, were:

- Unicentric
- Retrospective: data were collected between 2020 - 2021 for patients who were followed between 1 January 2013 - 31 December 2019
- Non-experimental: the study did not influence the therapeutic management of rheumatic disease or pregnancy management
- Descriptive: the study described the followed group in accordance with the proposed objectives

Based on the purpose and the specific objectives of the study, the following eligibility criteria were identified:

- Patients with rheumatic / gastrointestinal disease diagnosed before pregnancy
- Patients followed throughout pregnancy and postpartum
- Patients of whom evolution of rheumatic/ gastrointestinal disease was monitored during pregnancy
- Presence in the observation sheets of all the necessary anamnestic, clinical and paraclinical information

The study was carried out respecting the rules in force on scientific research valid at national level (Law 206/2004) and at a European level (The European Code of Conduct for Research Integrity and the Helsinki Declaration).

RESULTS

The study group is made of 70 patients with ages between 19 and 43 years, with an average of 31.95 years and a median of 32 years. The maximum number of cases was in the age range of 30-35 years with a number of 35 pregnant woman.

A central element of the analysis in the present study is the underlying autoimmune rheumatic/gastrointestinal disease, a disease diagnosed before pregnancy according to international specific diagnostic criteria. We note that the autoimmune diseases included in the study were: Crohn's disease (7 cases), lupus (11 cases), rheumatoid arthritis (27 cases), Sjogren's syndrome (8 cases), rectocolitis (9 cases), antiphospholipid syndrome (3 cases) and ankylosing spondylitis (1 case). Three patients associated two diseases: rheumatoid arthritis and Sjogren's syndrome (2 cases), respectively antiphospholipid syndrome and lupus (1 case).

Regarding to the age at diagnosis of the underlying rheumatic disease, there is an interval of the age of diagnosis between 12 and 32 years, with an average of 23.72 years and a standard deviation of 5.09 years. In most patients, the diagnosis was made after the age of 20.

Out of the total of 70 patients included in the research, 2 used In Vitro Fertilization, so that in the case of the other 68 patients the pregnancy could be obtained naturally.

19 patients from the study group representing 27.14% had at least one pregnancy loss. From these 19 patients with pregnancy loss 10 have had only one pregnancy loss, 3 patients with 2pregnancy loss and 3 patients with 4 pregnancy loss, 2 patients with 3 pregnancy loss, and 1 patient with 7 pregnancy loss.

During pregnancy, the patients included in the research gained a number of kilograms between 5 and 30 kg, with an average value of 12.46 kg and a standard deviation of 4.74 kg. The distribution of cases in relation to weight gained, shows a maximum number of cases in the range of 10-12 kg and an uneven distribution in regard to the initial weight with a gain between 11.11% and 47.61%.

The time interval between the diagnosis of the underlying rheumatic disease and the pregnancy had an average value of 8.05 years, with a range of values of 1 to 19 years, and a standard deviation of 4.84 years.

Regarding the time elapsed from the last recurrence of autoimmune disease at the time of pregnancy, the average value was 13.84 months with a standard deviation of 13.48 months and a range of values from 0 to 84 months.

Table 1 presents the percentage distribution of cases in relation to the activity score of the underlying disease in 5 moments of pregnancy's evolution: preconception, in each trimester of pregnancy and postpartum. Therefore, most patients were in remission or presented low activity disease at the time of conception (64 from 70 cases), so their percentage decreased with advancing pregnancy - 65 cases in the first trimester, 57 cases in the second trimester, 53 cases in the third trimester, and 36 cases postpartum.

	Remission	Low	Moderate	High
Preconception	40	24	5	1
1st Trimester	37	28	5	0
2nd Trimester	35	22	11	2
3rd Trimester	33	20	10	7
Postpartum	19	17	20	14

Table 1 – Distribution of cases in relation to the activity score of the underlying rheumatic disease

The graphic presented in Figure 1, highlights the worsening of underlying rheumatic disease during pregnancy with an emphasis on moderate and increased activity in the postpartum period (34 cases), compared to 17 cases in the third trimester.

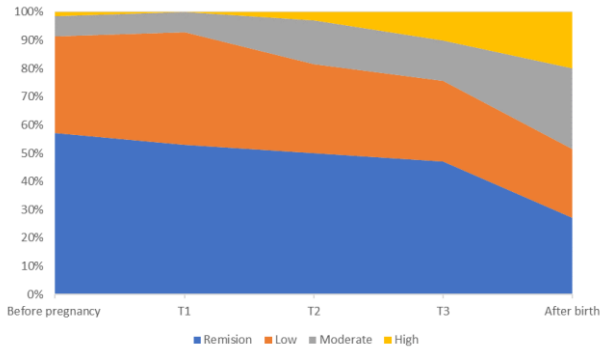

Figure 1 – Dynamic percentage distribution of cases in relation with the activity score of the underlying rheumatic disease

During pregnancy, 23 patients suffered from a relapse of the autoimmune disease. The onset time of exacerbation during pregnancy varied between week 4 and week 35 of pregnancy, with a median value of 28 weeks. Most relapses were recorded after the 20th week of pregnancy.

	Relapse (weeks)
Mean	27.174
Median	28.000
Std. Deviation	7.215
Variance	52.059
Range	31.000
Minimum	4.000
Maximum	35.000

Table 2 – Statistical data regarding the time of relapse of rheumatic disease in relation to the pregnancy's evolution

Regarding the mode of delivery out of the 70 patients included in the research, 50 gave birth by cesarean delivery and the remaining 20 gave birth by vaginal delivery. 12 cesarean deliveries were emergencies: 4 cases of premature membrane rupture (PROM), 3 cases of hypertension crisis, 1 eclamptic crisis and 5 cases of fetal distress, representing 26% from all cesarean deliveries in the study group. 16 patients out of 70 have developed pregnancy induced hypertension (22,85%), and 11 from this subgroup have developed preeclampsia (15.71%).

Considering the gestational age, the birth occurred for all patients between the 34th and 40th week of pregnancy, with a median value of 38 weeks. Most births took place in week 38 (22 cases), respectively week 39 (21 cases). 8 patients have had preterm births representing 11,42% from the study group, preterm birth being define as birth under 37 weeks of gestation.

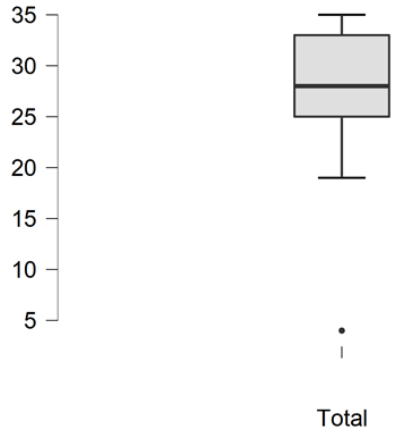

Figure 2 – Statistical data regarding the time of relapse of autoimmune disease in relation to the pregnancy's evolution

Out of a total of 70 patients included in the research there was only a stillbirth, representing 1.42%, the other 69 fetuses being viable.

Regarding the birth weight of the offspring from mother with autoimmune diseases the majority of newborns were normal weighed for the gestational age, with the mean weight of 2974.55 g and a standard deviation of 542.29 g.

As for Apgar score of the newborns, for the majority of cases – 47/70, Apgar score at 1 minute was 9. 14/70 Cases had a score of 9, 8/14 of 8, 2/70 of 7 and 2/70 of 6.

DISCUSSION

We can conclude the fact that women with autoimmune diseases have a prolonged time to achieve pregnancy and that in most cases, they will have an activity flare during pregnancy or postpartum even though they were in remission or presented low activity disease at the time of conception [2], [7], [10], [11]. Throughout pregnancy, rheumatic diseases need to be monitored closely in order to receive adjunct treatment, while obstetricians need to identify any fetal abnormalities in order to plan the best timing for delivery and avoid perinatal morbidity and mortality [2], [12].

The lack of data concerning management of the preconception, pregnancy and postpartum evolution and consequent complications caused by autoimmune diseases, especially rare ones, make medical counselling and treatment decisions complex, constraining specialists into creating individualized plans in order for women to achieve pregnancy and maintain it and for controlling the activity of the underlying disease [10], [13], [14]. There is also a need for creating pregnancy registers and developing studies in order to compare disease-match groups [15], [16].

CONCLUSIONS

The awareness regarding reproduction in women with rheumatic diseases made pregnancies possible and with fewer complications along the way, imputing interdisciplinary management and pre-conceptional counselling. Pregnancy complications as pregnancy loss, cesarean delivery, preeclampsia, intrauterine growth restriction, preterm birth are more often among pregnant women with autoimmune diseases, but severe complications like perinatal deaths and structural malformation are rare. The take home message of these research is that pregnancy in woman with autoimmune diseases should be multidisciplinary monitored due to possible placental transfer of maternal autoantibodies, the possible effects of maternal medications on the fetus and the newborn.

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