



Original article

## Pregnancy outcomes in dermatomyositis and polymyositis patients

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ABSTRACT

**Background:** Currently, there are few studies that describe pregnancy in dermatomyositis/polymyositis patients, and they are largely limited to case reports or studies with few samples.

**Objectives:** Therefore, we describe the pregnancy in a large sample of patients with dermatomyositis/polymyositis and to analyze the outcomes in those who became pregnant during or after disease onset.

**Methods:** The present single-center study analyzed 98 female patients with idiopathic inflammatory myopathies (60 dermatomyositis and 38 polymyositis patients). They were interviewed to obtain obstetric antecedent and demographic data from June 2011 to June 2012.

**Results:** Seventy-eight (79.6%) of the 98 patients had obstetric histories. Six polymyositis and 9 dermatomyositis patients became pregnant after disease onset. The pregnancy outcomes in these cases were good, except in the following cases: 1 disease reactivation, 1 intrauterine growth retardation, 1 diabetes mellitus, 1 hypertension, 1 hypothyroidism, and 2 fetal losses (same patient). Moreover, 2 patients developed dermatomyositis during pregnancy and 4 (2 polymyositis and 2 dermatomyositis) during the postpartum period with good control after glucocorticoid and immunosuppressant therapy.

**Conclusions:** The adverse obstetric events were related to clinical intercurrences and the pregnancy does not seem to carry a worse prognosis specifically in disease (for example: disease relapsing). Moreover, dermatomyositis or polymyositis onset during pregnancy or the postpartum period had good outcome after drug therapy.

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## Desfechos da gestação em pacientes com dermatomiosite e polimiosite

### RESUMO

**Palavras-chave:**

Dermatomiosite  
Miopatias inflamatórias  
Intercorrências obstétricas  
Polimiosite  
Gestação

**Introdução:** Há poucos estudos que descrevem a gravidez em pacientes com dermatomiosite/polimiosite. São, em grande parte, limitados a relatos de casos ou estudos com amostras pequenas.

**Objetivos:** Analisar a gestação em uma grande amostra de pacientes com dermatomiosite/polimiosite e os desfechos naquelas que engravidaram durante ou depois do início da doença.

**Métodos:** Foram analisados 98 pacientes do sexo feminino com miopatias inflamatórias idiopáticas (60 com dermatomiosite e 38 com polimiosite). Elas foram entrevistadas entre junho de 2011 e junho de 2012 para coletar seus antecedentes obstétricos e dados demográficos.

**Resultados:** Tinham antecedentes obstétricos 78 (79,6%) das 98 pacientes. Seis pacientes com polimiosite e nove com dermatomiosite engravidaram após o início da doença. O desfecho da gravidez nessas pacientes foi bom, exceto nos seguintes casos: um de reativação da doença, um de retardo do crescimento fetal, um de *diabetes mellitus*, um de hipertensão arterial, um de hipotireoidismo e dois de aborto (mesma paciente). Além disso, duas pacientes desenvolveram dermatomiosite durante a gravidez e quatro (duas polimiosite e duas dermatomiosite) durante o período pós-parto, com bom controle a seguir com glucocorticoides e terapia imunossupressora.

**Conclusões:** Os eventos obstétricos adversos estiveram relacionados com as intercorrências clínicas e a gravidez não parece levar especificamente a um pior prognóstico na doença (por exemplo: recidiva). Além disso, a dermatomiosite ou polimiosite de início durante a gestação ou no período pós-parto apresentou boa evolução depois do tratamento farmacológico.

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### Introduction

Dermatomyositis (DM) and polymyositis (PM) are systemic inflammatory autoimmune myopathies characterized by the subacute onset of symmetric weakness in the proximal musculature. Furthermore, cutaneous manifestations, such as heliotrope rash and Gottron's papules, are present in DM. Additionally, extra-muscular manifestations, such as articular, cardiorespiratory and gastrointestinal abnormalities may be found in both diseases.<sup>1,2</sup> The annual incidence of DM/PM is 0.5–8.4 cases per million habitants, affecting twice as many women as men, with no racial predilection. The DM affects both children and adults, whereas PM is seen after the forth decade of life and very rarely in childhood.<sup>3–5</sup>

Various studies conducted worldwide have assessed pregnancy in systemic rheumatic diseases. In systemic lupus erythematosus, for example, the maternal mortality risk is 20 times higher than that of a healthy pregnant female. These women also have a high risk of cesarean delivery, preterm labor, preeclampsia, thromboembolic events, and infectious and hematological complications.<sup>6</sup> For rheumatoid arthritis, various studies have shown improvement of symptoms during pregnancy.<sup>7</sup> However, especially in active rheumatoid arthritis, there is a slight increase in the rate of children with decreased birth weight and gestational age.<sup>8</sup>

Currently, there are few studies that describe pregnancy in DM/PM patients, and they are largely limited to case reports or studies with small samples.<sup>9–27</sup> Thus, little is known about the effects of pregnancy on DM/PM, whether these patients find

it harder to conceive or if pregnancy outcomes are adversely affected by myositis. Herein, we evaluate pregnancy in a large sample of DM/PM patients and describe the outcomes in those who became pregnant during or after disease onset.

### Materials and methods

The present retrospective cohort study was performed at a single center and included 98 consecutive DM/PM patients ( $\geq 18$  years old) from June 2011 to June 2012. All patients met at least four of the five Bohan and Peter criteria items,<sup>28</sup> and they were regularly following at our myopathy unit of our tertiary care center from 1993 to 2012. Patients with other associated systemic autoimmune disease were not included in the present study.

The study was approved by the local ethics committee, and all of the study participants signed an informed consent form.

All of the participants underwent a standardized interview, and their medical charts were extensively reviewed. The following data were collected: basic demographic data, age of disease onset, treatment, number of pregnancies before and after disease onset, activity of the disease during pregnancy and pregnancy outcomes.

### Therapy

The patients were initially treated with corticosteroids (oral prednisone, 1 mg/kg/day), with later gradual dose reduction according to clinical and laboratory stability. When

disease was severe (progression of dyspnea, dysphagia, significant loss of muscle strength), pulse therapy with methylprednisolone (1 g/day for three consecutive days) was performed. The following corticosteroid sparing agents were used as monotherapy or in combination: methotrexate (20–25 mg/week), azathioprine (2–3 mg/kg/day) or cyclosporine (2–4 mg/kg/day), chroloquine diphosphate (3–4 mg/kg/day), and cyclophosphamide (0.5–1.0 g/m<sup>2</sup> of body surface). The cyclophosphamide was used in the presence of progressive dyspnea associated with pulmonary parenchymal change confirmed on computed tomography ("ground-glass" opacity of honeycombing).

### Statistical analysis

The data are expressed as the mean and standard deviation (SD) for continuous variables or as frequencies and percentages for categorical variables.

### Results

Obstetrical history was noted in 78 (79.6%) out of 98 women with DM/PM (Fig. 1). Of these, 57 women, who were not described in this study, had a pregnancy before the onset of DM/PM.

Of the remaining patients, 15 became pregnant after disease diagnosis; whereas 2 women developed the disease during pregnancy and 4 postpartum mothers developed DM/PM. In total, there were 50 pregnancies, and 10 women had a history of miscarriage. Twelve patients had 2–7 pregnancies, and 1–4 pregnancies occurred before the DM/PM diagnosis.

The average age of pregnant women with established disease was  $30.6 \pm 3.7$  years (range 22–37 years), with a mean duration of disease of  $13.4 \pm 4.3$  years. There were 9 cases of DM and 6 PM in a total of 21 pregnancies. Among the clinical complications, there were 2 fetal losses, 1 case of intrauterine growth retardation, 1 case of decompensated gestational diabetes mellitus, 1 case of systemic arterial hypertension, 1 case of decompensated hypothyroidism and 1 case of venous thrombophilia. Only 1 case had worsening disease status, for

which corticosteroids were reintroduced, and good disease control was achieved. Four patients received corticosteroids throughout pregnancy with good clinical and laboratory disease control (Table 1).

In 2 cases, the disease (DM) developed during the pregnancy (Table 2). Particularly in the patient n° 16, the corticosteroid was started two months later, since the cutaneous lesions were initially attributed to allergic reaction and the progressive muscle weakness was not so clinically evident.

In four cases, DM/PM were diagnosed in the postpartum period (Table 3).

### Discussion

Herein, we assessed pregnancy in a large sample of DM/PM patients and the outcomes in those who became pregnant during or after disease onset.

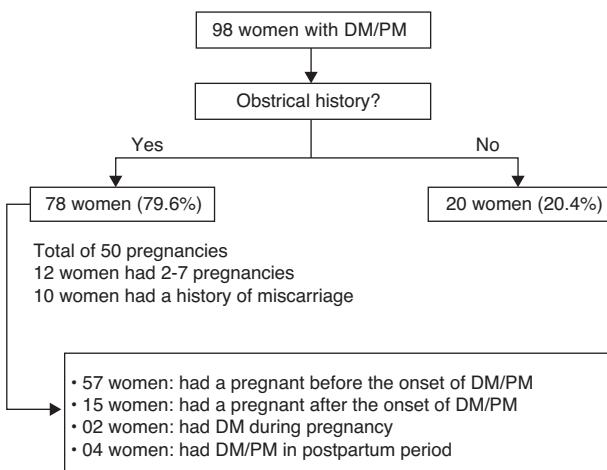
There are various studies that analyze pregnancy in systemic rheumatic diseases, but not in DM/PM. Hence, the present study contributed to the few available studies in the literature. Moreover, the advantage of this study was the analysis of obstetric antecedents in a large sample of DM/PM patients.

There are two types of pregnancy-related myositis: one presenting during pregnancy and the other, less common, developing postpartum. In the present study, we did not consider the outcomes of pregnancies that occurred prior to the diagnosis of DM/PM.

The evolution and behavior of pregnancy in inflammatory myopathies that are either active or in remission is still controversial in the literature. There is, for example, a description of pregnancy in patients with frank DM/PM activity. However, with the introduction of drug therapy, the disease is controlled without complications after delivery.<sup>9–13</sup> England et al.<sup>16</sup> reported a case without neonatal complications but resulting in maternal death due to acute exacerbation of diabetes. Silva et al.<sup>29</sup> reported eight cases of disease development postpartum. Gutierrez et al.<sup>30</sup> observed three patients with previously inactive disease that had an exacerbation during pregnancy. Other studies have reported illness after childbirth or abortion, suggesting that the fetus acts as a foreign body, perpetuating disease activity only during pregnancy.<sup>18–21</sup> In this study, all patients had stable disease, and 4 patients used corticosteroids to control the myopathy during pregnancy. In contrast, only 1 case demonstrated clinical and laboratory reactivation of the disease requiring corticosteroids, but with good control of disease activity. From the obstetric standpoint, with the exception of 6 cases, successful pregnancies without feto-maternal complications were the rule in the peripartum period.

There are few studies involving a large enough sample to allow generalizations about pregnancy in DM/PM patients.<sup>9,29–32</sup> Based on these studies, the main obstetric complications described are intrauterine growth retardation, prematurity and fetal death.

In the present study, 2 women had three pregnancies after disease onset. In 1 PM patient, gestational diabetes developed in the third pregnancy. However, there was no reactivation of disease in the peripartum or postpartum period. In the second



**Fig. 1 – Description of dermatomyositis and polymyositis patients.**

**Table 1 – General characteristics of pregnancy outcomes in dermatomyositis and polymyositis patients.**

ID	Mother's age (years)	G/P/A	Maternal adverse event	Disease	Disease duration prior to pregnancy (years)	Disease status at pregnancy	Previous therapy	Current therapy (at pregnancy)	Gestational age (week)	Fetus weight (g)	Fetal adverse event
1	33	6/0/5	Venous thrombophilia	DM	12	Stable	MTX 25 mg/week, AZA 3 mg/kg/day, CD 4 mg/kg/day	CD 4 mg/kg/day	32w2d	2090	Healthy
1	35	7/1/5	Hypothyroidism	DM	14	Stable	MTX 25 mg/week, AZA 3 mg/kg/day, CD 4 mg/kg/day	CD 4 mg/kg/day Pred 10 mg/day	37w3d	2410	Healthy
2	30	2/1/0	Healthy	DM	6	Stable	AZA 3 mg/kg/day, CD 4 mg/kg/day	–			Healthy
2	35	3/2/0	Healthy	DM	11	Stable	AZA 3 mg/kg/day, CD 4 mg/kg/day	–			Healthy
3	28	1/0/0	Healthy	DM	9	Stable	MTX 25 mg/week, AZA 3 mg/kg/day, CD 4 mg/kg/day	CD 4 mg/kg/day			Healthy
4	24	3/2/0	Healthy	DM	6	Stable	AZA 3 mg/kg/day	–			Healthy
5	22	1/0/0	Healthy	DM	18	Stable	AZA 3 mg/kg/day, CD 4 mg/kg/day	CD 4 mg/kg/day		3410	Healthy
6	33	1/0/0	Healthy	PM	12	Stable	AZA 3 mg/kg/day	Pred 20 mg/day		3180	Healthy
7	29	1/0/0	Healthy	DM	5	Stable	CYC 0.5–1.0 g/bs <sup>2</sup>	–		3420	Healthy
8	34	4/1/2	Healthy	PM	17	Stable	AZA 3 mg/kg/day	Pred 30 mg/day	39w1d	3090	Healthy
9	28	2/1/0	Healthy	PM	13	Stable	MTX 25 mg/week, CD 4 mg/kg/day	–			Healthy
9	30	3/2/0	Healthy	PM	15	Stable	MTX 25 mg/week, CD 4 mg/kg/day	–			Healthy
9	37	4/3/0	Diabetes mellitus	PM	17	Stable	MTX 25 mg/week, CD 4 mg/kg/day	–		3390	Healthy
10	31	1/0/0	Healthy	DM	13	Stable	MTX 25 mg/week	–			Fetal loss
10	32	2/0/1	Healthy	DM	14	Worse	MTX 25 mg/week	Pred 1 mg/kg/day			Fetal loss
10	34	3/0/2	Healthy	DM	16	Stable	MTX 25 mg/week	–	40w		IUGR
11	33	2/1/0	Healthy	PM	21	Stable	MTX 25 mg/week	–		3600	Healthy
12	30	1/0/0	Healthy	PM	19	Stable	MTX 25 mg/week, AZA 3 mg/kg/day 20 mg/day	Pred AZA 3 mg/kg/day 20 mg/day			Healthy
13	29	3/2/0	Healthy	PM	13	Stable	MTX 20 mg/week	–		3200	Healthy
14	30	3/2/0	Healthy	DM	17	Stable	AZA 3 mg/kg/day	–			Healthy
15	26	2/1/0	Hypertension, healthy	DM	14	Stable	AZA 3 mg/kg/day	–			Healthy

BS, body surface; ID, identification; G, gravida (pregnancies); P, parity (births); A, spontaneous abortion; IUGR, intrauterine growth retardation.

Drugs: AZA, azathioprine; CD, chroloquine diphosphate; CYC, cyclophosphamide; MTX, methotrexate; Pred, prednisolone.

**Table 2 – Two dermatomyositis onset at the pregnancy.**

ID	Mother's age (years)	G/P/A	Maternal adverse event	Disease	Clinical and laboratory features	Therapy	Gestational age (week)	Cesarean delivery (w)	Apgar score	Fetus weight (g)	Fetal adverse event
16	29	1/0/0	Diabetes Hypertension	DM	Progressive symmetrical weakness muscle, heliotrope rash, Gottron's papules, creatine kinase 494 IU/L, aldolase 173 IU/L, electromyography (proximal limb myopathy)	After two months, Pred 1 mg/kg/day were started with good results. After parturition, AZA and subsequently, MTX and CP were associated with good disease control	24	37	8/9/9	3210	Healthy
17	26	1/0/0	Hypothyroidism	DM	Dysphagia, progressive symmetrical weakness muscle, heliotrope rash, Gottron's papules, creatine kinase 22858 IU/L, aldolase 159 IU/L, electromyography (proximal limb myopathy)	Pred 1 mg/kg/day. After parturition, MTX was associated with good disease control	25	38	9/10/10	3000	Healthy

ID, identification; G, gravida (pregnancies); P, parity (births); A, spontaneous abortion.

Drugs: AZA, azathioprine; CP, cyclosporine; MTX, methotrexate; Pred, prednisolone.

**Table 3 – Four dermatomyositis/polymyositis that were diagnosed in the postpartum period.**

ID	Mother's age (years)	G/P/A	Maternal adverse event	Disease	Clinical and laboratory features after parturition	Therapy	Cesarean delivery (week)	Apgar score	Fetus weight (g)	Fetal adverse event
18	35	3/0/0	–	PM	Two months after parturition: progressive symmetrical weakness muscle, creatine kinase 2300 IU/L, aldolase 29 IU/L, electromyography (proximal limb myopathy), muscle biopsy consistent with an inflammatory myopathy	Five months after symptom onset, pred 1 mg/kg/day, AZA and MTX were initiated	40	9/10/10	3500	Healthy
19	32	3/0/2	Hypothyroidism	PM	Three months after parturition, progressive symmetrical weakness muscle, creatine kinase 12426 IU/L, aldolase 175 IU/L, electromyography (proximal limb myopathy)	Started immediately, pred 1 mg/kg/day, MTX, AZA. Symptoms improved after 8 months of clinical drug therapy	36	–	–	Fetal death (intrauterine fetal maceration and hypoxia)
20	24	1/0/0		DM	Two months after parturition, progressive symmetrical weakness muscle, creatine kinase 4100 IU/L, aldolase 45 IU/L, electromyography (proximal limb myopathy), heliotrope rash, Gottron's papules	Started immediately, pulse therapy with methylprednisolone (1 g/day for three consecutive days), followed by pred 1 mg/kg/day plus cyclophosphamide. Subsequently, initiated AZA and MTX with good disease control.	39	9/10/10	3200	–
21	25	2/0/0		DM	One month after parturition, progressive symmetrical weakness muscle, creatine kinase 22,000 IU/L, aldolase 45 IU/L, electromyography (proximal limb myopathy), heliotrope rash, Gottron's papules	Started immediately pred 1 mg/kg/day plus AZA, CP and MTX with good disease control	39	9/10/10	3300	–

ID, identification; G, gravida (pregnancies); P, parity (births); A, spontaneous abortion.

Drugs: AZA, azathioprine; CP, cyclosporine; CYC, cyclophosphamide; MTX, methotrexate; Pred, prednisolone.

case, a patient with DM, there were 2 fetal losses; during her second pregnancy, she experienced disease reactivation as previously mentioned. In the third pregnancy, she had intrauterine growth retardation, but with stable disease. In general, there were no significant pregnancy complications in our sample, probably because the majority of patients had stable disease.

Concerning fertility, it has been suggested that the rates are significantly different before and after the onset of DM/PM.<sup>9</sup> However, the late age of onset and the use of contraceptives preclude an accurate evaluation of the influence of the disease on fertility. Different follow-up periods, lack of information on the use of contraception and a scarcity of cases also make this analysis difficult. In the present study, 6 patients had new pregnancy after the onset of DM/PM. Moreover, one of them had two pregnancies after disease onset.

In the present study, in four cases, DM/PM onset occurred during the postpartum period. In all of these cases, there was good control of the disease after the introduction of corticosteroids and immunosuppressive drugs. Kofteridis et al.<sup>14</sup> described an acute onset of diabetes in pregnancy that lead to rhabdomyolysis and fetal loss. Autoimmune disease may be induced as a result of maternal hormonal changes, alteration of immune function during pregnancy or as a consequence of maternal exposure to fetal antigens,<sup>33</sup> which may explain the onset of DM/PM in the postpartum period.

There are some limitations to the present study. Our study is limited by its retrospective cohort study design. Furthermore, this work includes the characteristics of the study population, which were from a tertiary care center and most likely represent a more severe disease spectrum; therefore, the frequency of pregnancy and its repercussions in DM/PM might not have been well-estimated.

## Conclusions

The adverse obstetric events were related to clinical intercourses and the pregnancy does not seem to carry a worse prognosis specifically in disease (for example: disease relapsing). Moreover, dermatomyositis or polymyositis onset during pregnancy or the postpartum period had good outcome after drug therapy.

## Conflict of interest

The authors declare no conflicts of interest.

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