Pregnancy-Related Complications in Patients With Fibromuscular Dysplasia

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A Report From the European/International Fibromuscular Dysplasia Registry

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on behalf of the European/International Fibromuscular Dysplasia Registry and Initiative (FEIRI) and the Working Group "Hypertension and the Kidney" of the ESH

Abstract—Current literature suggests a higher risk of pregnancy-related complications in patients with renal fibromuscular dysplasia (FMD). The aim of our study was to assess the nature and prevalence of pregnancy-related complications in patients subsequently diagnosed with FMD. A call for participation was sent to centers contributing to the European/International FMD Registry. Patients with at least 1 pregnancy were included. Data on pregnancy were collected through medical files and FMD characteristics through the European/International FMD Registry. Data from 534 pregnancies were obtained in 237 patients. Despite the fact that, in 96% of cases, FMD was not diagnosed before pregnancy, 40% of women (n=93) experienced pregnancy-related complications, mostly gestational hypertension (25%) and preterm birth (20%), while preeclampsia was reported in only 7.5%. Only 1 patient experienced arterial dissection and another patient an aneurysm rupture. When compared with patients without pregnancy-related complications, patients with complicated pregnancies were younger at FMD diagnosis (43 versus 51 years old; $P<0.001$) and had a lower prevalence of cerebrovascular FMD (30% versus 52%; $P=0.003$) but underwent more often renal revascularization (63% versus 40%, $P<0.001$). In conclusion, the prevalence of pregnancy-related complications such as gestational hypertension and preterm birth was high in patients with FMD, probably related to the severity of renal FMD. However, the prevalence of preeclampsia and arterial complications was low/moderate. These findings emphasize the need to screen hypertensive women for FMD to ensure revascularization before pregnancy if indicated and appropriate follow-up during pregnancy, without discouraging patients with FMD from considering pregnancy. **(*Hypertension*. 2020;76:545-553. DOI: 10.1161/HYPERTENSIONAHA.120.15349.)** ● **Data Supplement**

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Fibromuscular dysplasia (FMD) is an idiopathic, segmental, nonatherosclerotic, and noninflammatory disease of the musculature of the arterial walls, leading to stenosis of small- and medium-sized arteries.[1,45] It affects predominantly middle-aged women, involving more frequently renal and cerebrovascular arteries and often presenting with hypertension.[1,45] Both endogenous and exogenous female hormones have been studied as potential risk factors for FMD because of its female predominance. However, to date, firm evidence of an association between FMD and female hormones or oral contraceptive therapy is lacking.[2–4]

While chronic hypertension is clearly associated with an increased risk of superimposed preeclampsia,[5–8] fetal growth restriction, preterm birth, and cesarean section,[8] data on pregnancy-related complications in patients with FMD are scant and mostly based on case reports.[9–15] To our knowledge, only 1 single-center retrospective study[16] looked for the prevalence of preeclampsia in patients subsequently revascularized for renal artery stenosis. In patients with FMD-related renal artery stenosis, an alarming prevalence of preeclampsia of 51.9% was identified, versus 20% for atherosclerotic renal artery stenosis. Furthermore, irrespective of the presence of FMD, it has been assumed that the risk of aneurysm rupture and arterial dissection is increased during pregnancy and in the postpartum period, with potentially life-threatening consequences.[17–19] In particular, spontaneous coronary artery dissection (SCAD) occurring during pregnancy or in the postpartum is associated with more acute presentations and high-risk features than SCAD occurring in other circumstances.[20] These findings may be relevant, as SCAD has been associated to extracoronary FMD in 30% to 80% of cases.[21,22] Accordingly, the International FMD Consensus[1,45] has advised preconceptional counseling and follow-up in a specialized context for patients with FMD who are contemplating pregnancy, particularly in those with a history of arterial dissection or poorly controlled hypertension. However, the prevalence and nature of pregnancy-related complications in patients with FMD has never been studied on a wide scale.

The aim of our study was to assess the nature and prevalence of pregnancy-related complications in patients subsequently diagnosed with FMD and enrolled in the European/International FMD Registry.

Methods

The authors declare that all supporting data are available within the article and in the Data Supplement.

In December 2018, a call for participation was sent to investigation centers contributing to the European/International FMD Registry and Initiative.[23] More information on the European/International FMD Registry and Initiative (FEIRI) is available in Appendix in the Data Supplement. Only patients with an established diagnosis of FMD in any arterial bed and with at least 1 pregnancy were included in this analysis. FMD was defined as the presence of an idiopathic, segmental, nonatherosclerotic, and noninflammatory stenosis (either with focal or string-of-beads appearance) of a small- or medium-sized artery in at least 1 vascular bed, documented with computed tomographic angiography, magnetic resonance angiography, or catheter-based angiography imaging.[1,45] All patients meeting the inclusion criteria in each participating center were included in the overall dataset. Patients with a suspicion of FMD only based on duplex ultrasound or nulliparous were excluded. Patients whose primary diagnosis was SCAD were not eligible, even in the presence of extracoronary FMD lesions. Miscarriages occurring before 12 weeks of pregnancy were not taken into account.

All clinical investigators were provided with a 48-item dataset jointly developed by experts in FMD (A. Persu, A.J., A. Prejbisz, A.H.E.M.M.) and obstetricians (P.K., F.D.), aiming to assess the prevalence and characteristics of pregnancy-related complications (ie, preterm birth, gestational hypertension, proteinuria, and seizures), maternal placental syndromes (ie, preeclampsia, HELLP syndrome, abruptio placentae, and intrauterine fetal death), arterial dissection (occurring either during pregnancy or within 3 months postpartum), and blood pressure (BP) control before, during, and within 6 months after pregnancy. To fill the dataset for each patient included in the study, clinical investigators collected data on pregnancy and peripartum complications through medical files. Only in case of missing information, patients were interviewed by using the corresponding 48-item questionnaire (Appendix in the Data Supplement). Data on demographic and FMD characteristics were collected through the FMD Registry.

Office BP was measured by a physician with an oscillometric semiautomatic or automatic sphygmomanometer according to the recommendations of the European Society of Hypertension (3 consecutive BP readings after 5 minutes of rest with at least 1-minute interval between them; the mean of the 3 measurements was used as BP reference value).[24,46]

Abnormal pregnancy was defined as the occurrence of any of the following complications: gestational hypertension or resistant hypertension during pregnancy, gestational diabetes mellitus, clinically relevant proteinuria (defined as proteinuria ≥300 mg in a 24-hour urine collection or ≥30 mg/mmol in a urinary spot[25]) or seizure, preterm delivery, preeclampsia, HELLP syndrome, abruptio placentae, intrauterine fetal death, and arterial dissection.

Gestational diabetes mellitus was defined as any degree of glucose intolerance with onset or first recognition during pregnancy[26]; gestational hypertension was defined as de novo hypertension occurring after 20 weeks of gestation without clinically relevant proteinuria[25]; preeclampsia was defined as new hypertension occurring after 20 weeks of gestation with clinically relevant proteinuria[25]; HELLP syndrome was defined as the clinical condition characterized by severe preeclampsia with hemolysis, elevated liver enzymes, and low platelet count[27]; abruptio placentae was defined as the premature detachment of the placenta from the uterine wall before birth and after 20 weeks of gestation[28]; resistant hypertension was defined as office systolic BP ≥140 or diastolic BP ≥90 mm Hg despite 3 antihypertensive drugs at optimal or best-tolerated dosage.[24,46] Finally, preterm birth was defined as the birth of an alive baby before 37 weeks of pregnancy.

After resolution of all queries, statistical analysis was performed by using IBM SPSS Statistics, version 21.0 (IBM Corp, Armonk, NY). Continuous variables were expressed as mean±SD or median and interquartile range according to their distribution; categorical variables were expressed as percentages. Categorical variables were compared using the χ^2 test and continuous variables using Student *t* test or Mann-Whitney *U* test according to their distribution. $P<0.05$ was considered to be statistically significant.

Results

Demographic, Clinical, and FMD Characteristics

Fourteen centers volunteered to participate to the study for a total of 529 patients (Figure S1 in the Data Supplement). The full list of investigators and centers participating to the study is available in Appendix in the Data Supplement. Of 529 women enrolled in the European/International FMD Registry with an established diagnosis of FMD in any vascular bed, 237 had at least 1 pregnancy and were, therefore, included in the study. The main demographics and clinical characteristics of the overall cohort are shown in Table 1.

Included patients had a mean age of 48±14 years at diagnosis of FMD, with a mean body mass index of 25±5 kg/m^2 and a median serum creatinine of 0.85 (0.72–0.92) mg/dL, respectively. At the time of diagnosis of FMD, mean systolic and diastolic BP values were 138/84±24/14 mm Hg, with a median number of antihypertensive drugs of 1 (1-3). Current smokers were 23% with a median of 10 (5–13) cigarettes per day.

One hundred eighty-four patients (78%) had multifocal FMD and 91 (38%) had multivessel FMD, with 47 patients (20%) having FMD in 2 vascular beds, 31 patients (13%) having FMD in 3 vascular beds, and 13 patients (5%) having FMD in ≥4 vascular beds. In the subgroup of patients who underwent a full vascular screening for FMD in all vascular beds (187 of 237 patients; 79%), the prevalence of multivessel FMD was 49% (n=91).

Two hundred twelve of 232 women (91%) had renal FMD, 43% had cerebrovascular FMD, 39% and 23% of patients had FMD lesions in visceral and limb arteries, respectively. Only 1 patient had multifocal lesions in the left brachial artery.

Table 1. General and FMD Characteristics of the 237 Women With a Confirmed Diagnosis of FMD and At Least 1 Pregnancy, Enrolled in the European/International FMD Registry

Main Characteristics of Patients	Overall Population (n=237)
Age at FMD diagnosis, y	48.0±13.9
BMI, kg/m^2	25.2±5.1
Systolic BP, mm Hg	138±24
Diastolic BP, mm Hg	84±14
No. of antihypertensive drug classes	1 (1-3)
Serum creatinine, mg/dL	0.85 (0.72–0.92)
Multifocal FMD, %	184/237 (77.6)
Multivessel FMD, %	91/237 (38.4)
Presence of any aneurysm, %	72/237 (30.4)
Intracranial aneurysms, %	24/72 (33.3)
Presence of any dissection,* %	9/237 (3.8)
Renal artery FMD, %	212/232 (91.4)
Cerebrovascular FMD, %	82/192 (42.7)
Visceral FMD, %	57/146 (39.0)
Lower limb FMD, %	31/133 (23.3)
Interventions, %	127/237 (53.6)
Renal interventions	114/237 (48.1)
Cervical interventions	14/237 (5.9)
Other territories interventions	7/237 (3.0)
Surgical interventions	15/237 (6.3)
Endovascular interventions	121/237 (51.1)
Angioplasty	94/237 (39.7)
Angioplasty+stent	19/237 (8.0)
Aneurysm repair	22/237 (9.3)

BMI indicates body mass index; BP, blood pressure; FMD, fibromuscular dysplasia.

*Includes 1 case of spontaneous coronary artery dissection occurring in a patient with widespread extracoronary FMD.

Seventy-two patients (30%) had at least 1 aneurysm in any vascular bed, with a prevalence of intracranial aneurysms of 33% (24 of 72 patients), and 9 patients (4%) had at least 1 arterial dissection.

Finally, 127 of 237 patients (54%) underwent an interventional procedure at a mean age of 45±14 years (only 7 of 127 women were revascularized before the first pregnancy), most for hemodynamically significant FMD stenosis affecting renal arteries (n=114; 90%).

Pregnancy-Related Complications

We obtained data from 534 pregnancies (age at first pregnancy, 26±5 years; median of 2 [2–3] pregnancies/patient), with a total of 487 live births (median of 2 [1–2] live births/patient), defined as births ≥22 weeks or >500 g (Table 2).

In most women, FMD was diagnosed after pregnancy (in only 9 of 237, the diagnosis of FMD was made before the first pregnancy) with a median interval of time between the first pregnancy and FMD diagnosis of 21 (11–32) years.

Sixty-two patients (27%) had at least 1 miscarriage (n=86), defined as pregnancy loss <22 weeks, and 14% of women (n=30) had been already diagnosed with hypertension before pregnancy occurred (preexisting hypertension).

Of 93 women (40%) who experienced at least 1 complicated pregnancy, 55 patients (59%) had only 1 complicated pregnancy, 27 (29%) patients had 2 complicated pregnancies, and 9 patients (10%) had 3 complicated pregnancies. Only 2 patients had 4 (1%) and 5 (1%) complicated pregnancies, respectively.

Pregnancy-related complications mostly corresponded to gestational hypertension (25%) and preterm birth (20%). The prevalence of proteinuria and gestational diabetes mellitus were both low (8% and 2%, respectively), and no woman developed seizures during pregnancy. Preeclampsia was reported in 17 women (7.5%), at a mean age of 31±5 years, and occurred at a median of 31 (27–37) weeks of pregnancy (Figure 1). Among women with preeclampsia, the delivery occurred at a median of 31 (29–35) weeks, and the median birth weight of the newborn was 1752 (1018–2600) g. Only 2 patients (1%) presented with HELLP syndrome (mean age at the event, 30±9 years). Abruptio placentae and intrauterine fetal death occurred in 3 (1%) and 8 (4%) women, respectively (Figure 1).

Ten patients (5%) developed resistant hypertension during pregnancy; in 5 of them, it led to preterm delivery of the baby, and in 1 patient, to percutaneous angioplasty of a stenotic renal artery.

Only 1 patient with bilateral carotid and left vertebral multifocal FMD experienced an arterial dissection within 3 months postpartum. Nineteen days after delivery, she had intense headache with occipital pain, nausea, vomiting, vertigo, and dysarthria. The arteriography revealed a dissection of the left carotid and left vertebral arteries, with thrombosis of the basilar artery (Figure 2). Thrombolysis was performed without major consequences.

Another patient with focal renal FMD, preexisting hypertension and treated with α-methyldopa and labetalol during

Table 2. Prevalence and Nature of Pregnancy-Related Complications in the 237 Women With a Confirmed Diagnosis of FMD and At Least 1 Pregnancy, Enrolled in the European/International FMD Registry

Pregnancy-Related Complications	Overall Population (n=237)
No. of pregnancies/patient (not including miscarriages before 12 wk)	2 (2-3)
No. of live births/patient (≥22 wk or >500 g)	2 (1-2)
Women with at least 1 miscarriage, %	62/234 (26.5)
Assisted pregnancy (IVF)	9/231 (3.9)
Women with at least 1 abnormal pregnancy,* %	93/231 (40.3)
No. of abnormal pregnancies/patient experiencing at least 1 abnormal pregnancy	1 (1-2)
Preterm birth, %	45/224 (20.1)
Gestational hypertension, %	58/231 (25.0)
Known hypertension before pregnancy, %	30/212 (14.2)
Proteinuria any occurrence, %	14/218 (6.4)
Seizures any occurrence, %	0/229 (0)
Gestational diabetes mellitus, %	4/231 (1.7)
Preeclampsia, %	17/227 (7.5)
HELLP syndrome, %	3/230 (1.3)
Abruptio placentae, %	3/214 (1.4)
Intrauterine fetal death, %	8/215 (3.8)
Resistant hypertension during pregnancy, %	10/213 (4.7)
Leading to induction of labor	5/10 (50.0)
Leading to preterm delivery of the baby	6/9 (66.7)
Leading to renal revascularization during pregnancy	1/9 (11.1)
Arterial complications during pregnancy, %	1/230 (0.4)
Arterial complications within 3 mo postpartum, %	1/129 (0.8)
Office BP values after hypertensive pregnancy (at 6 mo)	
<140/90 mm Hg, %	78/108 (72.3)
>140/90 mm Hg, %	13/108 (12.0)
Unknown, %	17/108 (15.7)

BP indicates blood pressure; HELLP, hemolysis, elevated liver enzyme and low platelet syndrome; and IVF, in vitro fertilization.

*Abnormal pregnancy was defined as the occurrence of any of the following complications: gestational hypertension or resistant hypertension during pregnancy, gestational diabetes mellitus, clinically relevant proteinuria or seizure, preterm delivery, preeclampsia, HELLP syndrome, abruptio placentae, intrauterine fetal death, and arterial dissection.

pregnancy, experienced a subarachnoid hemorrhage due to the rupture of an intracranial aneurysm (2.6×3.0 mm) at 24 weeks of pregnancy, leading to coma and death of the newborn after urgent cesarean section.

When compared with patients without pregnancy-related complications, patients with complicated pregnancies were younger at FMD diagnosis (43±12 versus 51±13 years; $P<0.001$; Figure S2), had a lower prevalence of cerebrovascular (30% versus 52%; $P=0.003$) and lower-extremity FMD (12% versus 27%; $P=0.04$), and a lower prevalence of FMD-related aneurysms in any vascular bed (22% versus 36%; $P=0.02$) but more often underwent renal revascularization (63% versus 40%; $P<0.001$), despite no significant difference in terms of renal FMD involvement (93% versus 97%; $P=0.35$) or BP values (138/84±22/13 versus 137/84±27/15 mm Hg; $P=0.67/0.83$; Table 3). No differences in terms of pregnancy-related complications were found between patients with single and multivessel FMD (Table S1).

Discussion

We looked for the prevalence and nature of pregnancy-related complications in 534 pregnancies from 237 patients with FMD enrolled in 8 countries from Northern and Southern Europe. The main findings of our study are the following: (1) in 96% of patients, the diagnosis of FMD was made after pregnancy, with a time lag of 1 to 3 decades; (2) despite this time lag, 40% of women with FMD experienced at least 1 complicated pregnancy; (3) patients with complicated pregnancies were younger at FMD diagnosis, had a lower prevalence of cerebrovascular FMD and of FMD-related aneurysms, contrasting with a higher rate of renal artery revascularizations; (4) the most frequent complications were by far gestational hypertension (25%) and preterm birth (20%); (5) in contrast, the prevalence of preeclampsia (7.5%) and other maternal placental syndromes (4.6%) was moderate; (6) only 2 patients (<1%) experienced arterial complications: 1 left vertebral and carotid dissection and 1 rupture of an intracranial aneurysm.

The prevalence of gestational hypertension and preterm birth was 3-fold to 6-fold (25% versus 3.6%–9.1%)[28,30] and 2-fold (20% versus 5.5%–12.2%)[29,30] higher than in women from the general population, respectively (Figure 1; Table S2). The prevalence of preterm birth was slightly lower than in chronic essential hypertensive patients (20% versus 22.7%–33.3%)[7,8,29] (Figure 1; Table S2). In view of the earlier age at FMD diagnosis and of the higher rate of renal artery revascularization, contrasting with lower prevalence of cerebrovascular FMD, such complications may reflect the severity of FMD-related renovascular hypertension. Notably, hypertension became resistant in 4.7% of patients, leading to preterm induction of delivery in half of cases.

In contrast, the prevalence of preeclampsia was only moderately increased compared with the general population (7.5% versus 1.6%–4.0%)[28–30] but was substantially lower than in chronic hypertensive patients (22%–25.9%[7,8,29]; Figure 1; Table S2). The reasons for this difference are unclear and may be due to differences in the pathogenesis of essential and renovascular hypertension. Alternatively, it may reflect the fact that only part of patients with FMD had preexisting hypertension, and most of them were diagnosed with hypertension after delivery.

These results are in sharp contrast with the 51.9% prevalence of preeclampsia reported by Vance et al[16] in their retrospective study. This discrepancy may be explained by the fact that Vance et al only included patients undergoing renal revascularization, probably associated with more severe hypertension. Furthermore, this was a small (n=27) and single-center series, where information could be retrieved only in a minority of identified cases, and data collection was exclusively performed through phone calls using a 7-item questionnaire, with a large time gap between revascularization and data collection

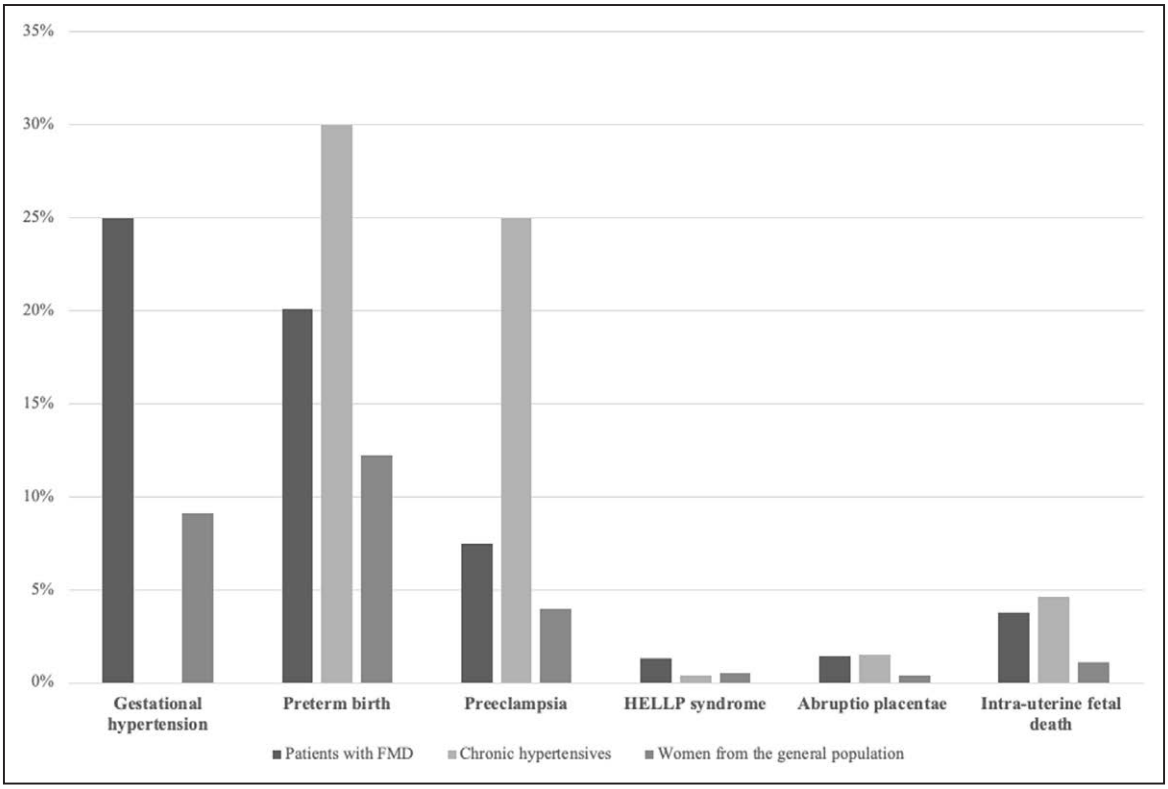

Figure 1. Prevalence of pregnancy-related complications and maternal placental syndromes in patients with FMD enrolled in the European/International FMD Registry, compared with patients with preexisting hypertension (known hypertension before pregnancy)[7,8,29] and with women from the general population[28–30] in historical cohorts (when a range exists, the upper estimate has been displayed). HELLP indicates hemolysis, elevated liver enzymes and low platelet count.

(6.9±3.6 years). These characteristics leave the door open for selection and recall biases. In contrast, in our study, data from 237 women from 14 European centers were mostly collected from medical files, while patients were interviewed only in case of missing information by using a detailed 48-item questionnaire (Appendix in the Data Supplement). Finally, our dataset includes a wide range of clinical presentations, and demographic and FMD characteristics were similar to those of the overall cohort enrolled in the European/International FMD Registry.[1–23,45] In view of the rarity of maternal placental syndromes other than preeclampsia,[31–33] it is difficult to draw firm conclusions.

Despite existing reports of vascular complications during pregnancy in patients experiencing FMD,[10–15] we identified only 1 case of dissection and 1 aneurysm rupture during the peripartum (overall prevalence <1%). While this finding is reassuring, such rare complications may nevertheless have life-threatening consequences, as shown in the second case where intracranial aneurysm rupture led to coma, with preterm delivery and death of the newborn.

The pathophysiologic mechanisms underlying the association between FMD and pregnancy-related complications remain unclear. Intriguingly, in a large majority of cases, FMD was diagnosed only years or even decades after pregnancy, though this diagnosis was made significantly earlier in patients with complicated pregnancies. The retrospective character of this study does not allow distinguishing patients with undiagnosed renovascular hypertension before pregnancy from patients with silent or preclinical FMD with more subtle structural or functional vascular abnormalities. which may have not led to clinical manifestations before years outside the challenge of pregnancy. Besides high BP,[5–7] different factors may account for the shift from asymptomatic to symptomatic FMD during pregnancy: this may include between others increased inflammation,[34] pregnancy-related hormonal changes leading to microstructural changes within the arterial wall,[35] and changes in serum levels of several cytokines. In particular, higher plasma levels of TGF (transforming growth factor)-β1 and TGF-β2 were found both in patients with FMD[36] and in patients with preeclampsia. In the latter, TGF-β1 may play a crucial role by activating the endothelial cell pathway[37] or through regulation of systemic inflammation.[38,39] Despite such fragmentary evidence, further studies are warranted to explore the common mechanisms underlying FMD and pregnancy-related complications.

Limitations

In this study, we assessed for the first time the prevalence of preeclampsia but also other maternal placental syndromes and arterial complications in a wide European representative series of patients with FMD, using a detailed 48-item dataset (Appendix in the Data Supplement).

Still, this study has several limitations: (1) first and foremost, in the large majority of cases, FMD was diagnosed well after the pregnancies, limiting the ability to discern cause and effect. On the other side of the coin, this provides the opportunity to look into the natural prognosis of pregnancies in FMD patients

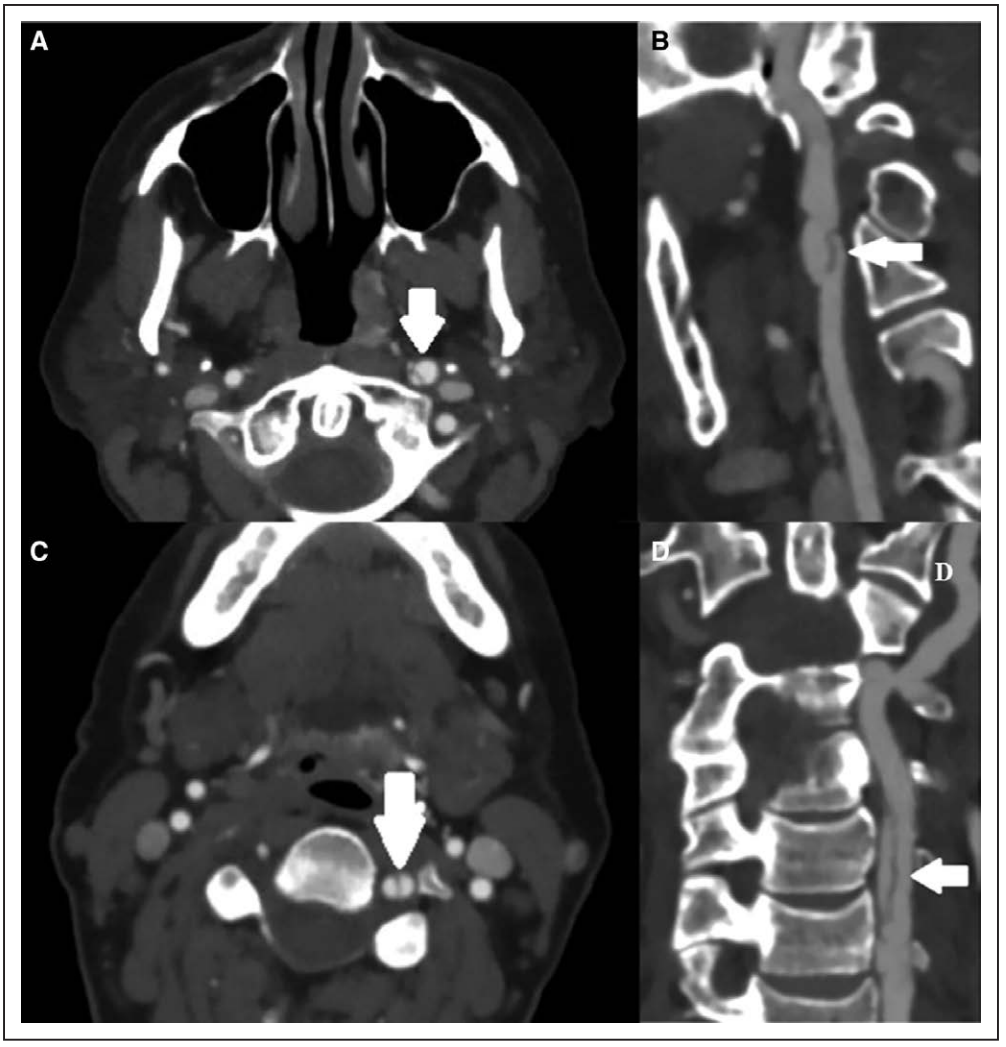

Figure 2. Postpartum dissection: carotid and vertebral dissection in a patient with multifocal fibromuscular dysplasia (FMD). Computed tomographic angiography showing cerebrovascular dissection occurring 19 d after delivery in a 36-y-old woman with multifocal FMD. **A**, Dissection (arrow) of the left carotid artery (cross section). **B**, Dissection (arrow) of the left carotid artery (midsagittal section). **C**, Dissection (arrow) of the left vertebral artery (cross section). **D**, Dissection (arrow) of the left vertebral artery (midsagittal section). In each figure, dissection is indicated by a white arrow.

without or with minimal intervention (in particular revascularization) before pregnancy; other limitations include (2) the risk of selection and recall bias due to the retrospective nature of the study and data collection from a registry—nevertheless, all patients from each participating center were enrolled, thus limiting selection biases. Furthermore, data on pregnancy-related complications were collected mostly through medical files; only a small subset of patients was interviewed by using a detailed questionnaire, thus limiting the risk of recall bias; (3) predominant inclusion of patients presenting with renal FMD, with underrepresentation of patients with cerebrovascular FMD or arterial dissection; (4) since patients with a primary diagnosis of SCAD were excluded from this study, our results cannot be readily extrapolated to SCAD patients.

Conclusions

In patients with FMD considering a pregnancy, appropriate management of hypertension, including adjustment of antihypertensive drug treatment and renal artery revascularization as needed, is recommended to limit the risk of severe, difficult-to-treat hypertension during pregnancy, leading to preterm birth and increased risk, both for the child and the mother. Our findings also further strengthen the recommendation of the International FMD Consensus[1,45] to perform a whole-body vascular screening in all patients with FMD to detect aneurysms or dissections that may be at the origin of rare but potentially life-threatening complications during the peripartum period. The impact of this approach on clinical decisions and management of patients with FMD has been recently documented in the Assessment of Renal and Cervical Artery Dysplasia-Poland (ARCADIA-POL) study.[40]

Furthermore, screening for renal artery FMD using state-of-the-art methods such as computed tomographic angiography or magnetic resonance angiography deserves to be considered in hypertensive women of childbearing age, especially in the absence of obvious explanations for hypertension (such as overweight, older age, or family history), to detect patients needing renal artery revascularization or management of aneurysm/dissection before pregnancy and ensure strict follow-up during pregnancy.[9,41] This is particularly true for women with early (diagnosed <30 years old), severe or resistant hypertension.[1,45]

Table 3. Differences in General and FMD Characteristics Between Patients With and Without Pregnancy-Related Complication(s)

Main Characteristics of Patients	Patients Without Pregnancy-Related Complications (n=142)	Patients With Pregnancy-Related Complications (n=93)	*P* Value
Current age, y	58.0±12.1	52.1±12.1	…
Age at FMD diagnosis, y	51.4±12.8	43.3±12.3	<0.001
BMI, kg/m^2	25.3±5.6	25.0±4.2	0.65
Office systolic BP, mm Hg	138±22	137±27	0.67
Office diastolic BP, mm Hg	84±13	84±15	0.83
No. of antihypertensive drug classes	2 (1-3)	2 (1-3)	0.20
Serum creatinine, mg/dL	0.85±0.24	0.86±0.25	0.70
Multifocal FMD, %	112/142 (78.9)	69/92 (75.0)	0.70
Multivessel FMD, %	59/141 (41.8)	31/92 (33.7)	0.21
Presence of any aneurysm, %	51/141 (36.2)	20/92 (21.7)	0.02
Presence of any dissection (including SCAD), %	6/141 (4.3)	3/92 (3.3)	0.70
Renal FMD, %	124/138 (97.1)	85/91 (93.4)	0.35
Cerebrovascular FMD, %	58/112 (51.8)	23/77 (29.9)	0.003
Visceral arteries FMD, %	35/89 (39.3)	22/56 (39.2)	0.99
Lower limb FMD, %	23/82 (28.1)	8/50 (16.0)	0.11
Interventional procedures, %	67/141 (47.5)	60/92 (65.2)	0.008
Renal intervention(s)	56/141 (39.7)	58/92 (63.0)	<0.001
Cervical intervention(s)	9/141 (6.4)	5/92 (5.4)	0.77
Other territory intervention(s)	4/141 (2.8)	3/92 (3.3)	0.85
Surgical interventions, %	8/141 (5.7)	7/92 (7.6)	0.56
Endovascular interventions, %	62/141 (44.0)	59/92 (64.1)	0.003
Angioplasty	46/141 (32.6)	48/92 (52.2)	0.003
Angioplasty+stent	9/141 (6.4)	10/92 (10.9)	0.22
Aneurysm repair	14/141 (9.9)	8/92 (8.7)	0.75

BMI indicates body mass index; BP, blood pressure; FMD, fibromuscular dysplasia; and SCAD, spontaneous coronary artery dissection.

Nevertheless, the yield and cost-effectiveness of systematic screening in this patient group remains to be demonstrated in large, multicentre prospective studies.

Finally, in agreement with the recommendation of the International FMD Consensus,[1,45] patients with FMD should benefit from a close follow-up during pregnancy and postpartum, involving an expert in FMD, as well as a high-risk obstetrician or maternal fetal medicine specialist. This is especially true for patients with severe or difficult-to-control hypertension, harboring aneurysms or dissections. Still, we feel that the relatively low prevalence of preeclampsia and severe maternal placental and arterial complications in this wide cohort is a reassuring message both for patients and caring physicians. In contrast with other arteriopathies such as vascular Ehlers-Danlos syndrome,[42] women with FMD should not be discouraged from considering pregnancy.

Perspectives

This study needs replication in a prospective multicenter cohort of women of childbearing age with FMD, including a balanced proportion of patients with renal and cerebrovascular FMD. Recruitment may be extended to patients with FMD and a history of SCAD. Ideally, it should also include a significant proportion of black patients, who are more prone to hypertension, gestational hypertension, and preeclampsia.[43] All patients should undergo head-to-pelvis computed tomographic angiography or contrast-enhanced magnetic resonance angiography before pregnancy as recommended.[1,45]

On the other hand, it would be interesting to look for the prevalence of renal artery FMD in patients diagnosed with hypertension during pregnancy, in the presence or absence of superimposed preeclampsia. Finally, as discussed previously, the implication of TGF-β–related pathways in the pathogenesis of both FMD and maternal placental syndromes deserves further investigation.[44]

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Novelty and Significance

What Is New?

- Compared with women from the general population, patients with fibromuscular dysplasia (FMD) have a substantially higher prevalence of pregnancy-related complications, particularly gestational hypertension and preterm birth.
- In contrast, the prevalence of preeclampsia is only moderately increased, and arterial complications (dissection, aneurysm rupture) appear to be rare, though the consequences may be severe.

What Is Relevant?

- In view of the increased rate of pregnancy-related complications in patients with FMD, screening for renal FMD deserves to be considered in hypertensive women of childbearing age, to detect patients needing renal artery revascularization and management of aneurysm/dissection before pregnancy.
- Still, as severe, life-threatening complications seldom occur, women with FMD should not be discouraged from considering pregnancy.

Summary

Data from 534 pregnancies were obtained in 237 patients with FMD enrolled in the European/International Fibromuscular Dysplasia Registry. Forty percent of women experienced pregnancy-related complications, mostly gestational hypertension (25%) and preterm birth (20%), while preeclampsia was reported in only 7.5%. Only 1 patient experienced arterial dissection and another patient, an aneurysm rupture. Patients with a history of complicated pregnancy were younger at FMD diagnosis, had a lower prevalence of cerebrovascular FMD, but underwent more often renal artery revascularization. Overall, the prevalence of pregnancy-related complications was higher than in historical cohorts of women from the general population but lower than in hypertensive women.