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Fabry Disease in Pregnancy: A Case Report

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ABSTRACT

Introduction: Fabry disease (FD) is an X-linked lysosomal deposit disorder caused by a deficiency in the enzyme lysosomal α-galactosidase A (α GAL-A) and the accumulation of globotriaosylceramide (Gb3) in the nervous, cardiovascular, and renal systems. Initially thought to be predominantly male, it has evolved to include heterozygous women with a diverse range of clinical symptoms. FD can pose health risks to the mother and her offspring during pregnancy, childbirth, and the neonatal period. The disease begins during the fetal stage of development, with most affected children remaining asymptomatic for the first few years. Progression of FD is associated with decreased renal function and proteinuria, and adults usually die prematurely due to organ failure. FD affects 1 in every 117,000 newborns, with an estimated prevalence between 1:40,000 and 1:117,000.

Clinical case: A 17-year-old Mexican female patient was diagnosed with Fabry's disease eight years ago, with no history of treatment. She had no history of drug or food allergies, no surgical history, and a history of renal failure due to Fabry's disease. The patient was hospitalized due to a 37.5-week term pregnancy, without labor, and no history of hypertensive disease in the pregnancy, threat of abortion, or preterm delivery. During hospital admission, medical evaluations were conducted by ophthalmology, cardiology, internal medicine, and psychology. The patient had no impairment of visual acuity, but had vascular tortuosity and glucosphingolipid deposits in the corneal stroma. The cardiac cavities were normal, and no significant valve diseases were found. The patient was asymptomatic at the time of admission and had a single delivery of a live newborn without apparent complications. Genetic monitoring was decided for an early diagnosis and timely pharmacological therapy to decrease comorbidities typical of Fabry's disease.

Discussion: Fabry disease (FD) is a rare chromosome-linked X-chromosomal disorder that alters lysosomal storage functions, caused primarily by mutations in the GLA gene encoding α-galactosidase A (α-GAL-A). It begins with cellular dysfunction and progresses over several years, eventually causing functional organ deterioration. Patients with FD experience multiple organ failure, with the kidneys, heart, and brain being the most susceptible organs. Initially predominantly male, women with FD have a diverse range of clinical symptoms and experience a level of clinical severity often equivalent to that observed in men. The onset of early symptoms and complications in adulthood tends to occur later in women. Pregnancies among women with

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FD revealed a higher prevalence of pregnancy-specific complications compared to the general population, but no life-threatening consequences were documented. Specific concerns related to women with FD during pregnancy involve the potential impact of microvascular disease, which can increase the risk of coagulation and exacerbate kidney function.

The burden of disease in pregnant women with FD is not well understood due to its low prevalence. Prenatal diagnosis of FD is usually made late due to the lack of initial specificity of the presentation symptoms. The first laboratory test is usually an assessment of GLA activity, with genetic analysis of mutations in the GLA gene being the gold standard. Prenatal diagnosis of FD can be achieved by demonstrating a karyotype XY and deficient α-GAL-A activity in chorionic villi or cultured amniocytes, or by prenatal molecular analysis if the fetus is female. The American Society of Genetic Counselors recommends fetal sex determination as the first diagnostic step in genetic counseling for families with a history of fetal deficiency (FD). Optimal management of pregnant patients with FD requires a dedicated multidisciplinary team. Enzymatic replacement therapy (ERT) is the cornerstone of comprehensive treatment, and early initiation is crucial for long-term benefits. The use of agalsidase alpha in pregnant women has been effective, but its efficacy may vary due to factors like age of onset and disease burden. Regular monitoring is essential for detecting early signs of disease progression.

Conclusion: Fabry disease affects women's quality of life and health system barriers, leading to delayed diagnosis and treatment. Despite its rarity and gender bias, individualized management during pregnancy is crucial. Enzyme replacement therapy should be evaluated in a multidisciplinary team. Family screening is essential for early diagnosis and management. Documenting treatments and results is crucial for future therapeutic decisions.

KEYWORDS: Fabry disease, lysosomal α-galactosidase, organ failure, pregnancy, α-galactosidase A, enzymatic replacement therapy, agalsidase, case report.

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INTRODUCTION

The Fabry disease (FD) is an X-linked lysosomal deposit disorder (Xq22.1), which results from a deficiency of the activity of the enzyme lysosomal α-galactosidase A (α GAL-A) with progressive accumulation of globotriaosylceramide (Gb3), mainly in the nervous, cardiovascular and renal systems. (1, 2)

It was first described by Johannes Fabry and William Anderson in 1898; initially thought to be predominantly male; due to X-chromosome heredity, heterozygous women were considered asymptomatic carriers; however, over time it has become evident that women have a diverse range of clinical symptoms and experience a level of clinical severity often equivalent to that observed in men. (3)

This hereditary, multi-systemic disease can pose health risks to the mother and her offspring during pregnancy, childbirth and the neonatal period. Only a few studies have reported pregnancy outcomes in women with FD, showing an increased incidence of proteinuria, preeclampsia, premature delivery, hypertension, miscarriage and intrauterine death. (4)

The activity of α GAL-A may be completely absent or low (<1%) resulting in the "classical" form of the disease, characterized by progressive and severe multiorgan involvement, or partially preserved (<30%) "late onset, not classical or atypical," characterized by isolated cardiac involvement or single organ damage. While plasma levels of liso-Gb3 appear to correlate with disease stages, mutation severity and decrease during Enzyme Replacement Therapy (ERT). (2, 5)

The primary process of disease eventually begins during the fetal stage of development; however, most affected children remain asymptomatic for the first few years of life while a cascade of events leading to tissue damage builds up. Progression of FD is commonly associated with decreased renal function and proteinuria. Adults usually die prematurely due to organ failure affecting the kidneys, heart and/or brain. (6)

FD is an unusual disease that affects 1 in every 117,000 newborns; however, recent data seem to show that the actual incidence could be higher, finding an estimated prevalence between 1:40,000 and 1:117,000. (1, 5)

FD predominantly affects men, with an incidence ranging from 1 in 40,000 to 1 in 170,000. Developed countries have started screening newborns for FD; but not all mutations result as clinically relevant. An affected woman who is heterozygous for the GLA gene mutation has a 50% chance of transferring an abnormal gene to both men and women. It is estimated that approximately 35% to 50% of FD patients worldwide have variants susceptible to GLA. (3, 8, 9)

Women who reported having pregnancies report experiencing early symptoms of the disease earlier, such as acroparesthesia, pain and gastrointestinal symptoms, these being the most common manifestations of the disease; as well as cardiac, renal, ophthalmologic and psychiatric symptoms compared to women without a history of pregnancy. Storage

of GL3 in placenta tissues derived from the mother and fetus has been documented, increasing the risk of constriction of placental blood vessels. No life-threatening complications such as kidney failure, stroke, acute myocardial infarction (AMI) or deep vein thrombosis (DVT) were reported during pregnancy. Children born to FD mothers were more likely to be premature or small for their gestational age. (4)

Since it is a multisystemic disease and the symptoms are nonspecific, there is usually a delay between the onset of symptoms and diagnosis of up to 10-15 years, this can have an impact on the health and quality of life of these patients. Sex, phenotype and plasma concentrations of Lyso Gb3 are strongly associated with the rate of clinical events. It is important to remember that the symptomatology is not specific, so care should be taken to attribute them directly to FD. (1,10, 11, 12, 13)

Cases of FD patients during pregnancy are rare and currently treatment is done individually and experimentally, so data on complications during pregnancy are scarce. In 2002, the American Society of Genetic Counselors recommended fetal sex determination as the first diagnostic step in genetic counseling for families with a history of FD. (14, 15)

We present the case report of a 17-year-old female patient diagnosed with FD during pregnancy

CLINICAL CASE

A 17-year-old Mexican female patient diagnosed with Fabry's disease 8 years ago in a genetic study, with no history of treatment because she was asymptomatic **(Table 1)**.

Table 1. Genetic study of the patient.

GENE NAME / ENZYME / BIOMARKER	OUTCOME	REFERENCE	INTERPRETATION
Lyso – Gb3	3.6 ng/ml	<1.8 ng/dl	pathological
GLA	Pathogenic variant heterozygous c.166T>C (p.Cys56Arg)	NM_000169.2	pathological

The patient had no history of drug or food allergies and no surgical history. Had a history of father who died from renal failure secondary to FD, and paternal grandmother who died from FD. As gynecoobstetric background: Menarche at 12 years of age and regular menstrual cycles.

The patient was hospitalized due to a 37.5-week term pregnancy, without labor, with a history of FD and no history of hypertensive disease in the pregnancy, threat of abortion or threat of preterm delivery.

During hospital admission, we kept a close watch on the binomial without reporting any eventualities; medical evaluations were made by ophthalmology, cardiology, internal medicine, and psychology for study protocol and multidisciplinary management, as well as to assess organic damage in the case of a multisystemic disease.

In the medical evaluations, there was no impairment of visual acuity; at the biomicroscopy, it presented vascular tortuosity and the cornea with deposits of glucosphingolipids in the corneal stroma. The fundus was reported unaltered, with no tortuosity, normal papilla and macula, and foveolar reflex present. Ocular disease in both eyes secondary to Fabry's disease, presence of tortuosity of conjunctival vessels, and presence of bilateral cornea verticillata. No ophthalmologic management was required, only indicating annual follow-up **(Image 1)**.

Image 1. Biomicroscopy, where the presence of deposits in the form of swirls is observed in the corneal epithelium.

The cardiac cavities were reported with normal dimensions, left ventricular geometry preserved, without alterations of mobility and segmental thickening of the left ventricle at rest, systolic and diastolic function of the ventricles without alterations, and without significant valve diseases **(Image 2)**. Systolic pressure of the pulmonary artery was 27 mmHg, with no evidence of pericardial effusion or intracavitary thrombus, excluding myocardial damage at that time

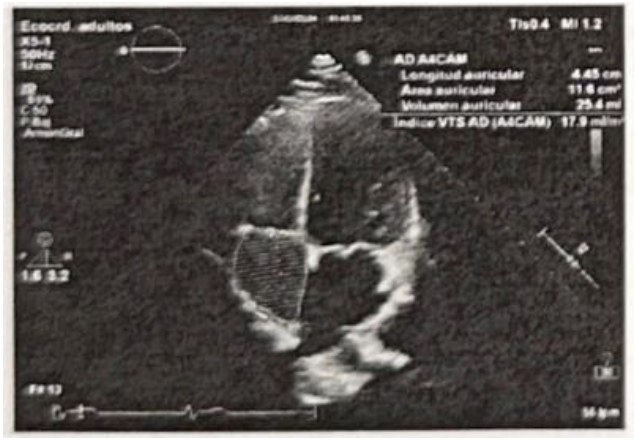

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Image 2. Apical four-chamber echocardiogram with parameters within the normal range.

Criteria of decompensation and impairment of renal function were excluded, as well as the diagnosis of anxiety, major depression and suicidal risk by psychology (Table 2).

Table 2. Report of laboratory studies.

	1ST TRIMESTER	2ND TRIMESTER	3ERD TRIMESTER	HOSPITALIZATION
HEMOGLOBINE	12.9	13	12.8	13.6
HEMATOCRIT	39.7	38	37.3	41.7
LEUKOCYTES	9.5	7.5	7.5	6.1
PLATELETS	280	220	168	163
BLOOD GROUP	O positive	-	-	-
TP	-	-	-	10.1
TTP	-	-	-	29.4
INR	-	-	-	0.87
GLUCOSE	77	68	-	67
UREA	9.3	0.4	-	9.4
CREATININE	0.6	0.4	-	0.4
URIC ACID	3.2	3.6	-	4.8
CHOLESTEROL	201	-	-	328
TRIGLYCERIDES	195	-	-	390
URINALYSIS	Leukocytes 6-8 Negative nitrites Protein negative Negative glucosuria	Normal	Normal	Leukocytes 20-25 Nitrites negative Protein negative Negative glucosuria Erythrocytes 0.1 Phosphate crystals ++
UROCULTIVE	-	No development	-	-
VAGINAL CULTURE	-	Candida SPP	-	-
HIV	Negative	-	-	-
VDRL	Negative	-	-	-
CTOG 75 GRAMS	-	Negative. 68/112/91/88.	-	-

At the time of admission to hospital, the patient was asymptomatic, with no data on low cardiac output or hypertensive encephalopathy, with adequate uresis, without alterations in gait. There was no dyspnea or pain related to

pregnancy, and no bleeding or transvaginal exudates; obstetric examination was performed without finding pathological signs.

The patient requested voluntary discharge on the same day of admission and went to the obstetric emergency room with 39.5 weeks of gestation, and in labor in active phase 10 days after her discharge. The maternal vital signs were found without alterations, amniorexis was performed at 6 cm of cervical dilation, finding clear amniotic fluid, normal fetal heart rate, with regular uterine activity.

Close surveillance of the maternal-fetal binomial was maintained, and a single delivery of eutectic vertex, without apparent complications, obtained a female live newborn with a weight of 2650 g, a size of 47 cm, an APGAR of 8/9, a Capurro of 38 weeks of gestation, a Silverman-Anderson of 0/0, a trivascular umbilical cord, and 200 ml of uterine bleeding.

The newborn was followed up for a neonatal cardiology examination and to rule out adjacent maternal disease, with no structural or functional alterations at that time; given the maternal and family history of Fabry's disease, it was decided to perform genetic monitoring for an early diagnosis and, if necessary, to initiate timely pharmacological therapy, to decrease comorbidities typical of this disease as a disorder associated with the metabolism of glucosphingolipids.

DISCUSSION

Fabry disease (FD) is a rare chromosome-linked X-chromosomal disorder that alters lysosomal storage functions, caused primarily by mutations in the GLA gene encoding α-galactosidase A (α-GAL-A). It begins with a cellular dysfunction, progressing over several years and eventually causing functional organ deterioration. These patients experience multiple organ failure, with the kidneys, heart and brain being the most susceptible organs. (3, 8)

Initially, FD was predominantly male, and women were regarded as asymptomatic carriers; however, over time it has become evident that women have a diverse range of clinical symptoms and experience a level of clinical severity often equivalent to that observed in men. The onset of early symptoms and complications in adulthood tends to occur later in women. (10)

A retrospective analysis of pregnancies among women with FD revealed a higher prevalence of pregnancy-specific complications compared to the general population; however, no life-threatening consequences associated with these complications were documented. Specific concerns related to women with FD during pregnancy involve the potential impact of microvascular disease, which can increase the risk of coagulation and exacerbate kidney function; storage of Gb3 in both maternal and fetal placental tissues has been observed, increasing susceptibility to constriction in placental blood vessels.Concomitant conditions, such as preeclampsia, gestational diabetes, hypertension, and maternal age at birth, can further complicate pregnancy in women with pre-existing FD. (3)

This hereditary, multi-systemic disease can pose health risks to the mother and her offspring during pregnancy, childbirth, and the neonatal period. During pregnancy, the most common signs and symptoms related to FD include proteinuria, acroparesthesia, headache, constipation, and diarrhea. Children born to mothers with FD are more likely to be premature and low birth weight, as well as being small for gestational age with more than double the frequency. (4)

In this case, it was observed that the patient had a normal pregnancy without obstetric complications associated with the gestation. However, it was identified that the newborn had a low growth percentile, which classifies it as small for gestational age.In male fetuses, Gb3 deposition has been demonstrated in glomerular endothelial cells, liver cells, mesenteric plexus cells, and the cornea; therefore, the primary disease process presumably begins during the fetal stage of development; however, most affected children remain asymptomatic during the first years of life as a cascade of events builds up leading to tissue damage. (6)

There are two types of FD presentation, classical and non-classical. The first consists of symptoms characteristic of FD, such as neuropathic pain, whorled cornea, and angiokeratoma, and long-term manifestations include hypertrophic cardiomyopathy, cardiac rhythm disturbances, progressive renal failure, and stroke. And the non-classical form, also known as late onset or atypical, is characterized by a more variable disease course, where patients are less affected, and manifestations of the disease can be limited to a single organ. (12)

The burden of disease in pregnant women with FD is not well understood due to its low prevalence. They may also present cardiac involvement and evidence of structural cardiac damage, especially left ventricular hypertrophy cardiomyopathy (LVH) and mitral valve insufficiency, the latter contributing to a high morbidity and mortality rate, age of 47. Abnormalities of atrioventricular conduction, arrhythmias, coronary failure, and valve involvement are other potential symptoms of cardiac involvement. A variety of symptoms, such as peripheral neuropathy, pain, autonomic dysfunction, and central nervous system manifestations, have been associated with neurological involvement in women affected by FD. (3)

In this patient, multiple medical evaluations were requested to rule out white organ damage. The cardiology service did not identify any structural or functional abnormalities by means of an electrocardiogram and echocardiogram, and myocardial damage was ruled out at that time. No alterations were observed in the heart cavities or valves. However, the possibility that the patient may develop a potentially life-threatening cardiovascular complication in the future cannot be excluded, considering that cardiac conditions are the main cause of mortality in patients with FD. (6)

There is a high risk of patients developing neuropsychiatric symptoms such as depression, suicidal tendencies, and neuropsychological deficits; currently there is little research on how the disease affects pregnant women psychologically; a multidisciplinary approach to diagnosis and treatment is therefore important. The psychological service used different scales of evaluation to detect early risk of depression, anxiety, and suicidal ideation in the patient during gestation. (3)

Among the ophthalmologic manifestations, corneal deposits with a characteristic golden brown swirl pattern known as vortex keratopathy or verticillae cornea are included. The only clinical manifestation of the disease present in this patient was the appearance of verticillose cornea. (8)

Patients with renal variants experience proteinuria, microalbuminuria, and reduced glomerular filtration rates, which can ultimately lead to kidney failure; the mean age of onset has been observed at 38 years; therefore, levels of proteinuria should be monitored throughout the pregnancy and addressed using established clinical guidelines. The patient was monitored for renal function, without detecting any proteinuria during pregnancy. (8)

The diagnosis of FD is usually made late; due to the lack of initial specificity of the presentation symptoms, it has been documented that the diagnosis could have a delay of up to 15 years, causing irreversible organic damage. The first laboratory test is usually an assessment of GLA activity; if there is a known familial mutation, basic DNA analysis is recommended. Measuring the activity of α-GAL-A is not a reliable diagnostic criterion; genetic analysis of mutations in the GLA gene, which reveals pathogenic mutation in more than 97% of patients, is the gold standard. (3)

Additional clinical and biochemical tests are required, as well as a slit lamp examination to check for verticillate cornea. The absence of a family history of the disease does not necessarily rule out FD, as new pathogenic variants may also occur spontaneously (de novo mutations). Detection of elevated levels of Lyso Gb3 is useful to confirm the diagnosis. The same choice has been made for pre-implantation genetic screening and donor eggs, not because of infertility but to prevent its transmission. (3)

Prenatal diagnosis of FD can be achieved by demonstrating a karyotype XY and deficient α-GAL-A activity in chorionic villi or cultured amniocytes, and/or by prenatal molecular analysis if the fetus is female. In 2002, the American Society of Genetic Counselors recommended fetal sex determination as the first diagnostic step in genetic counseling for families with a history of FD, and couples at risk should receive genetic counseling. (15)

The clinical journey from initial clinical manifestations to diagnosis and appropriate treatment remains a challenge due to late recognition or total neglect. Optimal management of pregnant patients with FD requires a dedicated multidisciplinary team that covers everything from differential diagnosis to prevention of complications and timely assessment for disease-specific therapies. (16)

Enzymatic replacement therapy (ERT) is the cornerstone of comprehensive treatment of FD; published guidelines recommend that all women be considered for ERT in case of significant symptoms or evidence of progression of organ involvement. The most prominent organ affected is the heart, both in patients with non-classical and classical FD. Early initiation of therapy may be crucial to long-term benefits; the optimal duration of therapy is still unclear, requiring further research to address this issue; it is suggested to start before age 25 to prevent organ damage. Pregnancy should not be a contraindication for ERT in FD; however, there is currently a lack of clarity regarding the optimal time to start ERT in pregnant women. (6)

The use of agalsidase alpha in pregnant women has been administered without any adverse impact on either the mother or the newborn, but its efficacy may vary due to factors such as age of onset, burden of disease, and residual enzyme activity. However, the use and safety of migalastat during pregnancy is still uncertain. (3, 9)

In this case, the patient was not treated with enzyme replacement therapy because she had been asymptomatic since her diagnosis. However, given the multisystemic and progressive nature of the disease, it is essential to consider their family history and prioritize close post-pregnancy follow-up to prevent future complications.

Regular, thorough monitoring is a prerequisite for detecting early signs of disease progression; there have been improvements in FD awareness and understanding as well as diagnostic practices over the past decades. Increased awareness of the natural history of the disease and the consequences of late treatment initiation, encouragement of frequent comprehensive monitoring, and family genetic analysis can help identify patients at an earlier age. (17)

CONCLUSION

Women with Fabry disease face reduced quality of life and barriers in the health system, including late diagnosis and lack of recognition of their symptoms, partly due to the rarity of the disease and gender bias. Lack of medical awareness delays treatment, which can have serious consequences given the progressive nature of the disease.

Although FD does not appear to significantly increase the risk of gynecological or obstetric complications, management during pregnancy remains individualized. Enzyme replacement therapy has not shown adverse effects in pregnancy, but its use should be evaluated on a case-by-case basis in a multidisciplinary team.

Family screening is key to improving early diagnosis and optimizing management of this multisystemic disease. Given the limited number of cases in pregnant women, it is critical to document treatments and results to strengthen clinical evidence and guide future therapeutic decisions.

ETHICAL CONSIDERATIONS

In this case report, the identifying information has been removed from all patient-related data.

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CONFLICT OF INTERESTS

The authors declare no conflict of interest.

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REFERENCES

I. Arends, M., Wanner, C., Hughes, D., Mehta, A., Oder, D., Watkinson, O. T., Elliott, P. M., Linthorst, G. E., Wijburg, F. A., Biegstraaten, M., & Hollak, C. E. (2017). Characterization of classical and nonclassical fabry disease: A multicenter study. Journal of the American Society of Nephrology, 28(5), 1631–1641. https://doi.org/10.1681/ASN.2016090964

II. Barba-Romero, M. Á., Serena, J., Puig, J. M., Valverde C., V., Climent, V., Herrero, J. A., Huertas, R., & Torra, R. (2019). Clinical profile of women diagnosed with Fabry disease non receiving enzyme replacement therapy. Medicina Clinica, 153(2), 47–55. https://doi.org/10.1016/j.medcli.2018.10.039

III. Bouwman, M. G., Rombach, S. M., Schenk, E., Sweeb, A., Wijburg, F. A., Hollak, C. E. M., & Linthorst, G. E. (2012). Prevalence of symptoms in female Fabry disease patients: A case-control survey. Journal of Inherited Metabolic Disease, 35(5), 891–898. https://doi.org/10.1007/s10545-011-9447-9

IV. Crea, F. (2024). New light shed on Anderson–Fabry, peripartum, and early-onset cardiomyopathies. In European Heart Journal (Vol. 45, Issue 16, pp. 1379–1383). Oxford University Press. https://doi.org/10.1093/eurheartj/ehae226

V. Del Franco, A., Iannaccone, G., Meucci, M. C., Lillo, R., Cappelli, F., Zocchi, C., Pieroni, M., Graziani, F., & Olivotto, I. (2024). Clinical staging of Anderson-Fabry cardiomyopathy: An operative proposal. In Heart Failure Reviews (Vol. 29, Issue 2, pp. 431–444). Springer. https://doi.org/10.1007/s10741-023-10370-x

VI. Germain, D. P., Bruneval, P., Tran, T. C., Balouet, P., Richalet, B., & Benistan, K. (2010). Uneventful pregnancy outcome after enzyme replacement therapy with agalsidase beta in a heterozygous female with Fabry disease: A case report. European Journal of Medical Genetics, 53(2), 111–112. https://doi.org/10.1016/j.ejmg.2009.12.004

VII. Haninger-Vacariu, N., Anastopoulos, K., Aigner, C., Sunder-Plassmann, R., Gatterer, C., Ponleitner, M., Sunder-Plassmann, G., & Schmidt, A. (2024). Pregnancy outcomes of Fabry disease in Austria (PROFABIA)-a retrospective cohort-study. Orphanet Journal of Rare Diseases, 19(1). https://doi.org/10.1186/s13023-024-03180-3

VIII. Haninger-Vacariu, N., El-Hadi, S., Pauler, U., Foretnik, M., Kain, R., Prohászka, Z., Schmidt, A., Skuban, N., Barth, J. A., & Sunder-Plassmann, G. (2019). Pregnancy Outcome after Exposure to Migalastat for Fabry Disease: A Clinical Report.

IX. Holmes, A., & Laney, D. (2015). A retrospective survey studying the impact of fabry disease on pregnancy. In JIMD Reports (Vol. 21, pp. 57–63). Springer. https://doi.org/10.1007/8904_2014_384

X. Izhar, R., Borriello, M., La Russa, A., Di Paola, R., De, A., Capasso, G., Ingrosso, D., Perna, A. F., & Simeoni, M. (2024). Fabry Disease in Women: Genetic Basis, Available Biomarkers, and Clinical Manifestations. In Genes (Vol. 15, Issue 1). Multidisciplinary Digital Publishing Institute (MDPI). https://doi.org/10.3390/genes15010037

XI. Kant, S., & Atta, M. G. (2020). Therapeutic advances in Fabry disease: The future awaits. In Biomedicine and Pharmacotherapy (Vol. 131). Elsevier Masson s.r.l. https://doi.org/10.1016/j.biopha.2020.110779

XII. Madsen, C. V., Christensen, E. I., Nielsen, R., Mogensen, H., Rasmussen, Å. K., & Feldt-Rasmussen, U. (2019). Enzyme replacement therapy during pregnancy in Fabry patients: Review of published cases of live births and a new case of a severely affected female with Fabry disease and pre-eclampsia complicating pregnancy. In JIMD Reports (Vol. 44, pp. 93–101). Springer. https://doi.org/10.1007/8904_2018_129

XIII. Martins, A. M., Cabrera, G., Molt, F., Suárez-Obando, F., Valdés, R. A., Varas, C., Yang, M., & Politei, J. M. (2019). The clinical profiles of female patients with fabry disease in latin america: A fabry registry analysis of natural history data from 169 patients based on enzyme replacement therapy status. JIMD Reports, 49(1), 107–117. https://doi.org/10.1002/jmd2.12071

XIV. Raas-Rothschild, A., & Lacombe, D. (2008). Fabry disease prenatal diagnosis. In Prenatal Diagnosis (Vol. 28, Issue 3, p. 268). https://doi.org/10.1002/pd.1942

XV. Raj, A., Sajayan, K., Chandran C, S., & Alex, A. T. (2024). Fabry disease management: Current status, therapeutic challenges, and future horizons in drug delivery and artificial intelligence assisted

diagnosis. In Journal of Drug Delivery Science and Technology (Vol. 100). Editions de Sante. https://doi.org/10.1016/j.jddst.2024.106032

XVI. Sánchez, R., Ripoll-Vera, T., López-Mendoza, M., de Juan-Ribera, J., Gimeno, J. R., Hermida, Á., Ruz-Zafra, M. A., Torregrosa, J. V., Mora, A., García-Pinilla, J. M., Fortuny, E., Aguinaga-Barrilero, A., & Torra, R. (2023). The Spanish Fabry women study: a retrospective observational study describing the phenotype of females with GLA variants. Orphanet Journal of Rare Diseases, 18(1). https://doi.org/10.1186/s13023-022-02599-w

XVII. Vardarli, I., Herrmann, C. R. K., & Weidemann, F. (2020). Diagnosis and screening of patients with fabry disease. In Therapeutics and Clinical Risk Management (Vol. 16, pp. 551–558). Dove Medical Press Ltd. https://doi.org/10.2147/TCRM.S247814