



CONSEQUENCES OF THE INTERACTION BETWEEN LEPROSY AND PREGNANCY REPERCUSSÕES DA INTERAÇÃO ENTRE HANSENÍASE E GRAVIDEZ

REPERCUSIONES DE LA INTERACCIÓN ENTRE LA LEPROSIA Y EL EMBARAZO

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ABSTRACT

Objective: to search and analyze the available evidence in the scientific literature that approached the maternal and fetal implications arising from the interaction between leprosy and pregnancy. **Method:** descriptive study, carried out in December 2011 through an integrative review of literature, in the CINAHL, MEDLINE and SCOPUS databases, by the research question "What are the implications of the interaction between leprosy and pregnancy for the woman and the baby?". Inclusion criteria were: articles available in full published in Portuguese, English, Spanish and French, with no temporal limits; answer the research question, resulting in eight jobs in the final sample. The data of the selected articles were condensed into a form that included article title, publication year, language, country of study, objectives, study design, and the results and conclusion highlights. A critical analysis of the sample was carried through the description of the related case report and meta-analysis. **Results:** all texts corresponded to the case study, 6 of them were Brazilian, but only 4 were diagnosed in Brazil. The previous contact with leprosy patients was reported in 3 cases. The disease was mainly diagnosed in the first trimester of pregnancy, and in 5 cases the fetus was born without changes. Lepromatous leprosy prevailed (5), and disabilities were registered in 6 cases. Leprosy reaction was present in 7 cases. **Conclusion:** we verified the importance of researching for signs of leprosy in pregnant women, making the differential diagnosis with other common skin changes in pregnancy. **Descriptors:** pregnancy, leprosy, health promotion.

RESUMO

Objetivo: analisar as evidências disponíveis na literatura que abordam as implicações maternas e fetais decorrentes da interação entre hanseníase e gravidez. **Método:** estudo descritivo, realizado em dezembro de 2011, por meio de revisão integrativa da literatura, nas bases de dados: CINAHL, MEDLINE, e SCOPUS, seguindo a questão de pesquisa: Quais as repercussões da interação hanseníase e gravidez para a mulher e o bebê? Os critérios de inclusão foram: artigos disponíveis na íntegra publicados em português, inglês, espanhol e francês; sem delimitação temporal; que abordassem a resposta a uma questão de pesquisa, resultando em oito produções na amostra final. Os dados dos artigos selecionados foram condensados em um formulário que abrangeu título do artigo, ano de publicação, idioma, país do estudo, objetivos, delineamento do estudo, destaques dos resultados e conclusão. A análise crítica da amostra foi realizada pela descrição do relato de caso relacionado, e a metanálise dos dados. **Resultados:** todos os textos corresponderam a estudo de caso, destes, seis eram de brasileiras, porém apenas quatro foram diagnosticadas no Brasil. O contato prévio com portador de hanseníase foi afirmado em três casos. A doença foi diagnosticada principalmente no 1º trimestre da gestação, e em cinco casos o conceito nasceu sem alterações. Prevaleceu a forma virchowiana (5), e incapacidades foram registradas em seis casos. Reação hanseníase esteve presente em sete casos. **Conclusão:** percebeu-se a importância da investigação de sinais de hanseníase em gestantes, realizando o diagnóstico diferencial com outras dermatoses comuns na gravidez. **Descritores:** gravidez; hanseníase; promoção da saúde.

RESUMEN

Objetivo: buscar y analizar las evidencias disponibles en la literatura científica acerca de las consecuencias maternas y fetales derivadas de la interacción entre lepra y embarazo. **Método:** estudio descriptivo, realizado en diciembre de 2011, mediante la revisión integradora de la literatura, en las siguientes bases de datos: MEDLINE, CINAHL, y SCOPUS, basado en la pregunta de investigación "¿Cuáles son las consecuencias maternas y fetales derivadas de la interacción entre lepra y embarazo?". Los criterios de inclusión fueron: artículos disponibles en su totalidad en Portugués, Inglés, Español y Francés, sin límites temporales, respuesta a la pregunta de investigación, resultando en una muestra de ocho artículos. Los datos de los artículos se condensaron en una forma que incluye el título del artículo, año de publicación, idioma, país, objetivos, diseño del estudio, y aspectos destacados de los resultados y conclusiones. Un análisis crítico se realizó a través de la descripción de caso y meta-análisis. **Resultados:** todos los textos correspondieron a estudio de caso, seis fueron de Brasil, pero sólo cuatro fueron diagnosticados en el Brasil. El contacto previo con los enfermos de lepra se afirmó en tres casos. La enfermedad fue diagnóstica principalmente en el primer trimestre del embarazo y en cinco casos, el niño nació sin cambios. Prevalció la forma virchowiana (5), y discapacidades se registraron en seis casos. Reacción de la lepra se presentó en siete casos. **Conclusión:** se percibió la importancia de la investigación de signos de la lepra en embarazadas, para el diagnóstico diferencial con otras dermatosis comunes en el embarazo. **Descriptores:** embarazo, lepra, promoción de la salud.

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INTRODUCTION

Health is recognized and promoted worldwide as the largest and best resource for the social, economic, and personal development, thus resulting in improved quality of life.

Since the 1970s, health promotion emerges as the basis of Public Health and, from then on, it has evolved and consolidated itself as a model for health actions. However, the current prevailing model in health generally consists of a fragmented practice, focused on individual cure of diseases, with a predominance of non-association between the numerous complaints from users and the related factors.¹

Using the principle of integrality, a new proposal contrary to the biomedical model emerges. Therefore, integral healthcare imply actions for health promotion, as well as prevention of diseases and risk factors, and then, once the disease is installed, proper treatment of patients is carried out; these actions are connected and distributed across all instances of the healthcare system.

Nowadays, leprosy is among the diseases deserving control measures, as well as ongoing and comprehensive monitoring, as it negatively affects the quality of life of patients, through disabilities resulting from it and social prejudice, which affect an increasingly young population with full reproductive ability.

Leprosy is an infectious disease caused by *Mycobacterium leprae*, a bacillus with high infectivity, low pathogenicity, and slow multiplication, a factor which reveals a variable incubation period, between 2 and 10 years, thus hampering early diagnosis. The major elimination routes of the bacilli in a patient are the upper airways, through intimate and prolonged contact to a person with multibacillary (MB) leprosy.³

The importance of immunological aspects in the prognosis of the disease is also recognized, especially with regard to what involves the emergence of leprosy reactions and neural damage, because the clinical signs are directly related to the individual's immune status, instead of the evolution of disease itself. Thus, circumstances causing changes in the balance between the bacillus and the host expose the patients to a greater risk. Among these conditions, stand out hormonal changes of puberty and pregnancy, which represent a physiological state of immunosuppression.^{4,5}

During pregnancy, the high levels of steroids, thyroid hormones, and estrogens cause a decrease in cellular immunity, more specifically of the Th1 type of cytokine in the response to lymphocytes, leading to a prevalence of the type Th2 in the response.⁶ This immunosuppression reverses around the 12th postpartum week, even in lactating women, changing the whole organic balance and with the possibility of leading to harmful effects on patients.⁴ This explains the pregnant woman's susceptibility to infections, and leprosy stands out among them, its Th1 and Th2 type responses are responsible for the clinical manifestations of disease.

According to the factors listed above, we emphasize the importance of an integral and specialized attention to women with leprosy. The World Health Organization (WHO) estimates that the proportion of number of cases is two cases in men for each woman with leprosy, however, this datum isn't confirmed in Brazil, because out of 38,894 new cases detected in 2010, 15,513 consisted of women.⁷

Women are concerned with deformities, since disabling lesions resulting from leprosy, besides making visible the disease, can contribute to a decline in the daily living, putting the patients' space at risk, whether within their family or at work. The non-fulfillment of their duties within the family shows the "inability" of their housekeeping and child care, reason for being abandoned by their partners. It leads to emotional distress and the sensation of amputating their attributes of competent women able to fulfill the tasks assigned to them, both inside and outside the family environment.⁸

Given the above and considering our experience in the care to patients with leprosy, with whom we share fears with regard to leprosy reactions, worsening of clinical condition, relapses, and neurofunctional impairments, associated to the disease and events which could intensify it, we identified the need for investigating the possible implications for the woman and the baby with an interaction between leprosy and pregnancy. Thus, we developed the following guiding question: What are the implications of the interaction between leprosy and pregnancy for the woman and the baby?

Hence, this study aims to analyze evidence available in the literature addressing maternal and fetal implications arising from the interaction between leprosy and pregnancy.

METHOD

Descriptive study carried out through an integrative literature review, which aims to gather and synthesize research findings on a theme or specific issues, such as systematic and structured methodology, contributing to a deeper knowledge on the theme under investigation.⁹

For the preparation of this integrative review, the following steps were taken: establishment of the hypothesis, aims, and criteria for inclusion and exclusion of papers in the sample; definition of the information to be extracted from selected papers; presentation and discussion of results; and the last step consists in the summary of the review.

The research question for the search of papers was: What are the implications of the interaction between leprosy and pregnancy for the woman and the baby? We used three databases as data collection sites, namely: *Cumulative Index to Nursing and Allied Health Literature* (CINAHL), MEDLINE/PubMed via *National Library of Medicine*, and SCOPUS. The descriptors used were *leprosy* (Hansen's disease) and *pregnancy*, in an integrated way, since it's a determination from the databases.

The search in the selected databases was done through the meta-search engine, which allows simultaneous search in these databases, enabled by the CAPES journals website, version 2011. The inclusion criteria were: papers fully available published in Portuguese, English, Spanish, and French; with no temporal boundaries; and addressing the consequences of the interaction between pregnancy and leprosy for the woman and/or the baby. The paper selection process was carried out through the reading of title and abstract. When these data were not enough, the full text was analyzed in order to check compliance with the inclusion criteria. The papers selected at this first moment had their data summarized into a form comprising the following information: paper's title, publication year, language, country where the study was carried out, aims, study design, highlights from the results, and conclusion.

The search, carried out on December 2011, resulted in a sample of 1,201 papers, distributed as shown in Figure 1. By reading the title, 233 papers were selected, but 70 were excluded because they were duplicated. After reading the abstract, 12 papers were selected. However, after reading the full text, 8 papers were included in the final sample of this study.

Bases	Total found	Selected by title	Excluded by repetition	Selected by abstract	Sample
CINAHL	9	3	70	12	8
PUBMED	197	82			
SCOPUS	995	148			
TOTAL	1201	233			

Figure 1. Papers selection process. CINAHL, MEDLINE, and SCOPUS; Dec. 2011.

For the synthesis and analysis of the papers which met the inclusion criteria, we used an electronic spreadsheet comprising the following aspects considered pertinent: research's title; reference's source; language of publication; country where the study was developed; case description; recommendations and/or conclusions; and critical analysis by the authors of this integrative review.

A critical analysis of selected papers was performed through a description of the case report concerned, and meta-analysis of data with the aim of comparing the information obtained, displayed in a table and in figures.

RESULTS AND DISCUSSION

All items had a case report design, and they have been grouped in order to highlight the relationship between leprosy and pregnancy, as shown in Table 1. Among the cases, 6 addressed Brazilian women, 4 women were diagnosed in Brazil, 2 in Germany, 1 in Spain, and 1 in France. Women's age ranged from 25 to 34 years, with an average of 31 years. None reported any previous treatment for leprosy. The time of signs and symptoms onset ranged from 2 weeks to 3 years before diagnosis.

Table 1. Distribution of cases according to gestational age of leprosy detection, clinical aspects of this disease, and conditions of the newborn infant. CINAHL, MEDLINE, and SCOPUS; Dec. 2011.

Variáveis (n=8)	n.
Gestational age of leprosy detection	
1st trimester of pregnancy	5
2nd trimester of pregnancy	1
1st trimester of lactation	2
OMS classification	
Multibacillary (MB)	7
Paucibacillary (PB)	1
Clinical form	
Lepromatous	5
Borderline	2
Tuberculoid	1
Degree of Functional Disability (DFD) in the diagnosis	
2	4
1	2
0	2
Type of leprosy reaction	
Erythema nodosum leprosum (ENL)	3
Reverse (RR)	2
Lucio's phenomenon	2
Showed no reaction	1
Clinical condition of the newborn infant	
No change	5
Not informed	2
Stillborn	1

Regarding the investigation on the period in which the disease was diagnosed, the first trimester of pregnancy prevailed, corroborating the critical period for the pregnant woman with leprosy reported in the literature, between the last trimester and the first three months of lactation, when immunosuppression reaches its peak.⁴

On the clinical and epidemiological findings of patients, there was predominance of lepromatous leprosy and, as a consequence, of the MB classification. In a descriptive, retrospective, study carried out with 183 leprosy patients treated at a healthcare center in Sao Luis, Maranhao, Brazil, the prevalent form in females was borderline (54.9%), followed by the tuberculoid and lepromatous, with 17.5% and 16.4% of cases, respectively.¹⁰ Perhaps, these conflicting results may be explained by the evidence of change in the immunity pattern during pregnancy or lactation, which contributes to the evolution of leprosy towards the lepromatous pole.¹¹

In 6 women, DFD 1 or 2 were shown in the diagnosis. An epidemiological study carried out in a town in Minas Gerais, comparing the values of the degree of disability according to gender in a sample of 2,333 leprosy patients, found a higher percentage of disability in males; one observed that 14% of cases had some degree of disability, an indicator considered high (> 10%), according to parameters from the Health Ministry. In the same study, a direct relationship between late diagnosis and increased DFD was found, since the late diagnosis after 2 or 3 years increased by 35% risk of disability, and when it is over 3

years, this risk rises to 48% when compared to early diagnosis, considered up to 2 years after the symptoms onset.¹²

The distribution of the leprosy reaction type was very homogeneous, with cases presenting an ENL, RR, and Lucio's phenomenon profile; one case had no manifestations. The effect of immunosuppression during pregnancy can precipitate the emergency of leprosy, relapse, leprosy reaction, as well as the development of resistance to dapsone, especially in the third trimester of pregnancy, with the emergence of ENL and RR after delivery.¹¹ This requires a special attention during pregnancy and during the next two postpartum years, to early detect a new reaction with possible neural damage.

RRs are directly connected to an increase in cellular immunity, occurring immediately after birth, peaking at 40 days later, and they emerge then in 50% of women for the first time. ENL can occur at any pregnancy stage due to the increased risk of intercurrent infections, which act as triggers for the episodes. However, their highest incidence occurs at the third trimester or at the immediate postpartum period, because of the emotional stress of childbirth and the sharp drop in plasma cortisol.⁴

The clinical condition of the newborn infant was mentioned in 6 cases, and there was one report of stillborn fetus whose mother had lepromatous leprosy (LL). In a study carried out from 1975 to 2003, with a prospective open cohort design, monitoring 156 women with leprosy and their children (generated during the presence of pathology),

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aiming to verify the implication of pregnancy concurrent with leprosy, found, with regard to the growth and development of these children, that women with leprosy have lower placenta and its function is deficient, the baby presents intrauterine growth retardation, low Apgar score, low birth weight, higher mortality, they are more susceptible to infections than babies whose mothers don't have leprosy, and these results

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are more pronounced in children whose mothers have lepromatous leprosy.¹¹

None of the papers mentioned the importance of postponing pregnancy during the presence of pathology and after hospital discharge or what contraceptive methods are suitable for the woman with leprosy. For a more comprehensive knowledge on the cases analyzed, we present a summary in Figure 2.

Case	Paper's title	Case report
1	<i>Lepra reaction and pregnancy.</i>	Woman, 34 years old, Brazilian, living in Spain, at the 2nd month of lactation, presented two weeks before painful erythematous plaques which stretched across the face and extremities, as well as edema and pain in her left foot. She reported to have a hypochromic spot on the right arm since her childhood, which suddenly grew and became erythematous and painful. Regarding previous contact to a person with leprosy, she worked in the care to patients with this disease for 4 years. Upon inspection, she showed numerous erythematous plaques, infiltrated, well-defined, with clear center, and alopecia on their surface, besides change in sensitivity. Thickening of peripheral nerves wasn't observed. Smear and Mitsuda tests showed negative results. In the end, she was diagnosed with tuberculoid leprosy (TL), and clinical profile compatible with RR. ¹³
2	<i>Concomitant Lucio phenomenon and erythema nodosum in a leprosy patient: clues for their distinct pathogeneses.</i>	Woman, 28 years old, Brazilian, living in Brazil, complained of purple bleeding lesions for three years. The first lesions emerged in lower limbs at the fourth month of her first pregnancy, which evolved without maternal and fetal complications. However, during the puerperium, lesions suddenly increased in number and size. Prior contact to patients with leprosy wasn't reported. Physical examination revealed diffuse infiltration, more evident on the face, elbows, and knees. Thickening and pain, in the ulnar and posterior tibial nerves, were also identified, with change in thermal sensitivity; madarosis, and partial loss of earlobe. The findings were consistent with a late stage of ENL, then the diagnosis of lepromatous leprosy was established. ¹⁴
3	<i>Leprosy in a pregnant woman.</i>	Woman, 29 years old, Filipino, living in Germany, at the 36th week of gestation, complained of pain in the joints, especially on both knees and ankles, which initially began as a mild pain, but became worse during pregnancy. She reported to have worked for one year as a nurse in the Philippines about 10 years before, but she couldn't refer to a previous contact to a leprosy patient. Examination revealed progressive rash and nodes along the extremities. Smear was positive, classified as a MB form. The child was born without any complication. ¹⁵
4	<i>Éruption de la face chez une femme enceinte.</i>	Woman, 34 years old, Cameroon, living in France, at the 12th week of gestation, had a rash on the face which emerged suddenly. The patient reported previous contact to family members with leprosy about 15 years before. Clinical examination revealed erythematous plaque on her left foot and two hypochromic and hypoesthetic lesions on the elbows and thighs, which, according to the patient, were there for seven months. She showed no nerve thickening. She presented negative smear. Determination of the leprosy form consisted in differing borderline-borderline leprosy (HBB) from lepromatous leprosy, and there was reverse reaction, according to the authors, probably triggered by pregnancy-induced immunosuppression. The delivery had no complications, and the child was born without changes. ¹⁶
5	<i>The Lucio's phenomenon (necrotizing erythema) in pregnancy.</i>	Woman, 27 years old, Brazilian, living in Brazil, at the 32nd week of gestation, presented erythematous-purpuric lesions on the limbs, well-defined, confluent, topped with bubbles, some of them necrotic and ulcerated, with one week of evolution, along with fever and intense pain at the site. She reported no previous contact to a leprosy patient. The smear was positive, showing globi, and skin histopathology confirmed lepromatous leprosy compatible with Lucio's phenomenon. Pregnancy progressed to vaginal delivery at term, without complications, the newborn infant had an appropriate weight for gestational age, and there was no malformations. ¹⁷
6	<i>Lucio's phenomenon (erythema necrotisans) in pregnancy: a case report and an overview.</i>	Woman, 25 years old, Brazilian, living in Brazil, at the 21st week of gestation, had large areas of dry skin necrosis, with irregular borders, affecting the face, trunk, upper and lower limbs, as well as erythematous-violet lesions with irregular borders in the face, madarosis, and ciliary rarefaction; there was no evidence of systemic or fetus compromise at the time of admission. She denied a previous contact to leprosy patients. Positive smear and histopathologic findings compatible with lepromatous leprosy and a characteristic profile of Lucio's phenomenon. She remained stable up to the 39th day of hospitalization, when she developed a profile compatible with the respiratory distress syndrome in adults, metabolic acidosis, and clinical and laboratory signs of acute liver failure. This was followed by premature delivery of stillborn fetus, with low birth weight, without external malformations. In less than 24 hours postpartum, the patient evolved to death, with shock and cardiopulmonary arrest. Histopathological examination of the placenta revealed a circulatory disorder characterized by diffuse congestion of the villi, intervillous hemorrhage, and some fibrin deposits. ¹⁸
7	<i>Erythema leprosum - after treatment of lepromatous leprosy.</i>	Woman, 33 years old, Brazilian, living in Germany, who have already been diagnosed with lepromatous leprosy and complained that, for months, painful nodules emerged on her face, chest, legs, and feet, along with ciliary and superciliary madarosis. Histology and smear test suggested the MB form. After

		one year of treatment, the patient decided to stop treatment to get pregnant. Two months after suspending the treatment, the patient returns at the 9th week of gestation complaining of joint pain and swelling in the joints, as well as painful and hemorrhagic nodules. The histological and clinical findings suggested ENL. The case worsened after delivery, with the emergence of new erythematous nodules. There was no record on the condition of the newborn infant. ¹⁹
8	<i>Leprosy simulating lichenoid eruption: case report and literature review.</i>	Woman, 39 years old, Brazilian, living in Brazil, complained of "wounds" in her body, about two years before, emerging as small nodules and widespread itching. She was treated with dexchlorpheniramine and betamethasone cream with gentamicin, presenting a partial improvement of the condition. After treatment, the patient got pregnant and relapsed with the emergence of numerous widespread pruritic lesions. She reported no previous contact with a leprosy patient. Dermatological examination showed numerous violaceous papular lesions on the trunk and limbs, some of them erythematous and other ones excoriated, resulting from the intense itching. The smear was positive, and histopathological examination revealed numerous bacilli and globi in the inflammatory process, characterizing borderline leprosy - lepromatous (BLL). The patient had a partial regression of clinical condition, after the fourth dose of the treatment. The patient didn't have a leprosy reaction. There was no record on the newborn infant's condition. ²⁰

Figure 2. Summary of the papers included in the integrative review. CINAHL, MEDLINE, and SCOPUS; Dec. 2011.

CONCLUSION

Faced with the evidence found, we highlight the importance of carefully monitoring a female patient with leprosy, advising on the risks to mother and baby in case of a concurrent pregnancy, in order to promote the adoption of contraceptive methods suitable for her. Another point to stress is the need for recognizing leprosy as a possible dermatologic disease presented during pregnancy, since there were several papers highlighting the prevalence of dermatoses during pregnancy, however, leprosy was marginalized.

The use of the Capes website as a search tool provided amplitude and quickness to the detection and analysis on the theme, however, the lack of free availability of full papers was a limitation of this study, an unfortunate fact, as in the sample found about 15 titles could enable a higher level of evidence for this review.

We hope that this study arouses the interest of researchers and professionals in the issue of contraception in fertile women with leprosy, because pregnancy should be a deferred event for this group, and that further studies can contribute to the prevention of pregnancy concurrent with leprosy, gathering safe contraceptive guidelines and presenting criteria for a healthy pregnancy after hospital discharge for leprosy.

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