PHD THESIS

CUTANEOUS MANIFESTATIONS INDUCED BY PREGNANCY. CLINICAL-EVOLVING (PROGRESSIONAL) STUDY AND THERAPEUTIC IMPLICATIONS

- SUMMARY -

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Summary

STATE OF KNOWLEDGE

CHAPTER I: Dermatosis induced by pregnancy. Definition and classification. Etiopathogenesis, risk factors.


Chapter III: Cutaneous changings induced by pregnancy.

PERSONAL CONTRIBUTIONS

CHAPTER IV: General clinical feature of the patients included in the study.


CHAPTER VII: Discussions.

CHAPTER VIII: Final conclusions.

BIBLIOGRAPHY

ANNEX

Keywords: dermatosis induced by pregnancy, risk factors, atopic field, directly and indirectly immunofluorescence, maternal and fetal prognosis.
Induced dermatosis of pregnancy are rare diseases, generally benign, except being Impetigo herpetiformis. They appear only during the gestation period, having different degrees of severity, disappearing after the expulsion of the conceptus and having the possibility to reoccur in a new pregnancy. The pathogenesis of dermatosis of pregnancy, except for Herpes Gestationis is still unknown. The risk factors, exogenous or endogenous, which are able to stimulate the emergence, relapse or worsening of these problems are: hormones (estrogen, progesterone), genetic predisposition, autoimmunity, sun exposure, age (under 20), liver disease, food deficiencies, anemia, hormonal disorders, infections and psycho-affective status of the pregnant women. Prurigo Gravidarum is the most common pruritic papulopustular dermatosis of pregnancy with an incidence of 2% in universal literature and approximately 0.8% in Europe. Acute Pruritus Gravidarum is considered a subtle form of intrahepatic cholestasis with a frequency of 1/10.000 of pregnant in the U.S.A., in Europe approximately 3% and 4-8% in South America. Papular Dermatosis of Pregnancy is rare, as well as Erythema Toxemia of the pregnant woman (frequency of 1 / 120 women with dermatosis). In Europe Pruritic Folliculitis of pregnancy has an incidence of 0.2%. One of the most common dermatosis of pregnancy, Urticaria of Pregnancy (Pruritic Urticarial Papules and Plaques of Pregnancy), has a frequency of 1/160-240 of pregnant women, affecting especially white women. Herpes Gestationis which affects especially white women, has an incidence which varies from statistics to another (1/3000-50,000), more frequent in Central Europe. Impetigo Herpetiformis is considered an exudative form of psoriasis with a particular evolution given by pregnancy and is rare. In the following decades, we consider that the study of these diseases will become a major public health concern because the prevalence of the atopic field and other risk factors involved in their etiopathogenesis.

This paper contains a number of 135 pages and is divided into two parts: one refers to the state of knowledge and other refers to personal contributions. The first part of the work entitled State of Knowledge contains a number of 36 pages dealing with current notions of the clinical description, paraclinical and differential for each dermatosis in hand, recent discoveries regarding the natural evolution, the treatment (remedy), maternal and fetal prognosis and classifications, definitions, etiopathogenesis and risk factors.

The second part of the work, referring to personal contributions has a number of 67 pages and is divided into three chapters which represents a clinical-statistical dermatosis induced by pregnancy personal research, study made on female patients who came in the Dermatology, Obstetrics and Gynecology Clinics and Internal Diseases of the County Emergency Hospital Craiova, aiming to establish correlations between the extent of injury, etiopathogenesis factors, clinical diagnosis, paraclinical, the remedy and the results.

The chapter entitled "General clinical features of the patients included in the study" was divided into subsections: Material, methods and results. The study was conducted within 5 years from 2005 to 2009 and included 167 patients. These were investigated anamnestic, clinical and paraclinical (laboratory tests, histopathology) examination, all data being passed in an evaluation sheet. I divided patients according to skin condition, area of origin, age and parity and I noticed that these dermatosis occur frequently on patients having their first pregnancy, from urban areas and with high education, aged from 21 to 40 years. From our research I noticed a low
frequency of dermatosis on pregnant who had twins, and a mismatch between the number of pregnant women who had Pruritic Urticarial Papules and Plaques and Prurigo Gravidarum compared to other skin manifestations induced by pregnancy. I watched the evolution of pregnancies noting that most were taken to term, resulting live newborns. The results were always compared with those described in the specialty literature, resulted from studies made by universities and research centers from Europe and the USA.

In the chapter entitled "Clinical-evolving aspects for dermatosis induced by pregnancy" I conducted a clinico-statistical analysis on the incidence of diseases, parity and gestational age at diagnosis, the way of appearance and the natural evolution. I evaluated, for each group studied, the factors involved in increasing the risk of occurrence of dermatosis, namely the presence of various allergies, the association of hypertension and weight gain over 15 pounds, prolonged exposure to sunlight (rural origin) and stress. I also analyzed the presence of family history and personal history of disease or disorders that occur or are favored by an atopic background. I watched the main symptoms through which manifested the studied dermatosis, the period from the symptoms appearance until the request for a medical specialized advice, and also the medical specialty where patients initially came. I attached great importance to paraclinical examination, laboratory tests, and also to histopathological examination. The aspects observed were compared to each other, but also with the normal appearance, knowing that in pregnancy appear a couple of changes which are considered as being normal. In diagnosing the case as Herpes Gestationis an important addition had, beyond the clinical appearance, and the anatomopathological examination, which revealed specific subcutaneous bag. The clinical and paraclinical aspects were illustrated with suggestive colored images.

In the chapter entitled "Therapeutic Implications" I conducted an extensive study of therapeutic attitudes. I described in detail the treatment used of each dermatosis, the pregnancy development, how it ends, also the weight and sex of newborns. The treatment applied locally and systemically focused on dermatosis but also on disorders of pregnancy’s evolution. I followed the association of various dermatological disorders induced by pregnancy with the way of their completion and I noticed that in most cases maternal and fetal prognosis was favorable, and the fact that some of the patients gave birth by caesarean section was not due to skin lesions but had obstetric causes. To illustrate the results, I used a demonstrative iconography and conclusive of high quality, represented by diagrams, tables, and original microphotos.

In the chapter ‘Discussions’ all the results obtained in our study are compared with those known from the literature of specialty, with data obtained from studies conducted by various centers and universities in Europe and the USA.

In the final chapter ‘FINAL CONCLUSIONS’ are rendered the final opinions of the thesis, with the practical implications in cutaneous pathology induced by pregnancy, emphasizing the contributors factors, the evolution and the treatment of dermatosis induced by pregnancy.

The „BIBLIOGRAPHY” impresses through its extensive documentation that includes a number of 170 authors, reference books from this field and also numerous new scientific articles and personal scientific papers published in the proceedings of the national and international scientific specialized events and articles published in scientific journals.

In the, ANNEX’ are listed my personal papers, in number of 6 –being published, which have as theme dermatological pathology during pregnancy, all referring to the issues covered in the PhD thesis.
CONCLUSIONS

- The results of this study realized on 167 pregnant women selected over a period of five years from 2005 to 2009 showed that 30% were diagnosed with Prurigo Gravidarum, Acute Pruritus Gravidarum 4%, 2% with Papular Dermatosis of Pregnancy, 3% Erythema Toxemia Gestationis, Pruritic Folliculitis 1%, 51% with Pruritic Papules and Plaques of Pregnancy, 7% with Herpes Gestationis, 2% with Impetigo Herpetiformis.
- The territorial distribution of patients showed a predominance of pregnant women with urban residence (69.47%) than in rural areas.
- In terms of age was observed that the majority of patients with Prurigo Gravidarum had between 21 and 30 years (46%) and Acute Pruritus Gravidarum (33.4%), Papular Dermatosis of Pregnancy (100%), Pruritic Folliculitis of pregnancy (100%). In the age group 31-40 years were found the largest number of pregnant women with Erythema Toxemia Gestationis (33.4%) with Urticarial Papules and Plaques of Pregnancy (48.24%) and Herpes Gestationis (75%). I have not found any pregnant with dermatosis autoimmune to progesterone.
- Regarding the cultural level it was observed the larger frequency to pregnats with higher education (64%) compared with the other.
- The distribution by parity of pregnants with pregnancy-induced disorders showed a predominance to women who were at first pregnancy (primiparous) (70%).
- In our study we have included three pregnants with twins (1.8%).
- The evolution of dermatosis and pregnancies was favorable, most pregnants gived birth on term (96.99%).
- Analyzing the risk factors suggestive for Prurigo Gravidarum I noticed that some of them are found to all women with pregnancy-induced dermatosis, while others are specific. I identified the risk factors of this disease: allergies (24%), stress (18%), antecedent history of allergy (6%) and primiparous (8%).
- Regarding the Acute Pruritus Gravidarum were involved the following risk factors: family history of disease (57.14%), sun exposure (28.57%), infection with hepatitis C (28.57%), infection with hepatitis B (14.29%), cholelithiasis (14.29%), primiparous (71.43%).
- Considering the incidence of allergies in the Papular Dermatosis of Pregnancy in the casuistry, I noticed that all pregnant women who experience this condition had an atopic background.
- I studied the involvement of allergy and Erythema Toxemia Gestationis and I noticed that 60% of pregnant women who were diagnosed with this condition were sensitive to dust. We also observed that 80% of pregnant women who developed this disease were primiparous and during pregnancy had taken over 15 kg weight.
- Pregnant women who had Pruritic Folliculitis were primiparous and the disease occurred after a stressful event.
- The assessment of risk factors in terms of Urticaria of Pregnancy showed that: weight gain over 15 pounds in 60% of women with this disease, hypertension, present in 50.59% of them, and various allergies to 44.70%. Most were in their first pregnancy (87.08%).
- The risk factors found to pregnants who had Herpes Gestationis were: stress (58.33%), sun exposure (41.68%), hypertension (41.68%), anemia and various vitamin deficiencies (41, 68%), personal history of disease (8.33%). All these patients were over 30 years.
Patients who developed Impetigo Herpetiformis during pregnancy were younger than 21 years, had allergies and were primiparous. 74% of pregnant women with Prurigo Gravidarum have come to the Dermatology Clinic for skin lesions and pruritus, the rest of them have come to the Department of Obstetrics and Gynecology for back pain or uterine contractions, the diagnosis of dermatosis being established after a dermatological consultation. The main reason that most patients with Acute Pruritus Gravidarum (71.4%) requested medical consultation in the Clinic for Internal Diseases was represented by scleral icterus.

Pregnant women with Papular Dermatosis have come to the doctor for a pruritic eritemo- papular rash, 33.3% presenting lesions on the face too.

Erythema Toxemia appeared during pregnancy determined the pregnant women to consult a doctor: 60% were submitted for consultation in the Dermatology Clinic with prurito eritemo- papular rash, and the other in the Clinic of Obstetrics and Gynecology for painful uterine contractions accompanied by back pains.

Patients with Pruritic Folliculitis of Pregnancy presented to the dermatologist for a rash consisting of small erythematous follicular papules very itchy. Pruritic Urticarial Papules and Plaques of Pregnancy determined that 85.89% of pregnant women who developed this condition to go to a dermatologist for the skin manifestations occurred.

75% of patients which developed during pregnancy Herpes Gestationis had been presented to the dermatologist for a pruritic rash, and the rest to the gynecologist.

Among pregnant women who have Impetigo Herpetiformis 66.7% came to the dermatologist.

Paraclinical evaluation of patients with dermatosis induced by pregnancy showed little changes to the parameters: in 58.68% of cases found Hb <10g% to 33.53% was evidenced eosinophilia, hypocalcaemia was observed in 61.68% of cases, 33.53% of women with dermatosis showed eosinophilia, hyperglycaemia was present in 2.99% of pregnant women, C-Reactive protein was detected in 1.20% of patients, hyperbilirubinemia was observed in 1.20% of cases, raised biliary acids to 3.59%, IgE increased to 27.54%, HCG increased to 1.80%, 9.58% of patients were diagnosed as carriers of HBs antigen, 5.39% were identified with antibodies C virus;

I performed biopsy with histopathology examination of the lesions and their vicinity, as well as direct and indirect immunofluorescence in all patients except those with Acute Pruritus Gravidarum. I observed that 75% of women with Herpes Gestationis in IFD was revealed the presence of IgG with C3 deposits located along the basement membrane, and with 25% of cases there have been found IgA, IgM, IgE, C4 and fibrinogen. IFI performed on pregnant women with Herpes Gestationis revealed the presence of HGF (herpes gestationis factor).

All pregnant women received adjuvant medication: antispasmodic, vitamins, sedatives. On 14% of women with Prurigo Besnier I used as topical therapy antipruritic menthol mixture 1% to 6% a mixture of anestezin 1% to 24% a preparation P1 (anestezin, ichtiol, zinc oxide, triamcinolone acetonide), from 36% a preparation P2 (anestezin, salicylic acid, urea, vitamin A), 20% P3 preparation (Nystatin, neomycin, anestezin, salicylic acid, urea, lucoid).

For patients with Acute Pruritus Gravidarum I used locally a mixture of mint and talcum powder, and systemic 42.86% cholestyramine, and to the others patients ursodeoxycholic acid 57.14%. 
For pregnant women with Papular Dermatosis I have administrated a topical mint mixture, and one patient took a short course of prednisone.

In 80% of pregnant women with Erythema Toxemia we used as local treatment based on a mixture of soot and 20% a dermatocorticoid.

For patients with Pruritic Folliculitis I indicated for the topic therapy dermatocorticoid.

In the treatment of pregnant women with Urticaria this was varied: from 63 of them I administrated in the treatment of Prurit a calming solution (menthol, glycerol, talc, zinc oxide, alcohol, hydrogen peroxide) and 61 of them I have added dermatocorticoid (triamcinolone acetonide), the other 23 I have given soot, 21 of them also received a dermatocorticoid (triamcinolone acetonide), I added to a single pregnant and prednisone.

Patients who developed Herpes Gestationis I have indicated a different treatment: two women have received soot and dermatocorticoid (triamcinolone acetonide), to 6 patients I have added oxymed to the soot; one pregnant received boric acid and oxymed, 2 patients have received boric acid and dermatocorticoid (triamcinolone acetonide), and a single patient received only dermatocorticoid (triamcinolone acetonide).

In the case of pregnants carring Impetigo Herpetiformis the treatment was complex. In addition to corticosteroids (prednisone) and antispasmodics, topical treatment consisted of aseptic with chloramine and dermatocorticoid (oxycort, betaderm).

The evolution of pregnant women with pregnancy-induced dermatosis was generally satisfactory. Of the 167 patients who gived birth prematurely, the rest carried the pregnancy to term and gave birth naturally 57.83% of them, the other by Caesarean section (performed for various obstetrical reasons).

The newborn babies of pregnant women with pregnancy-induced dermatosis were predominantly male (54.43%), generally healthy.
CURRICULUM VITAE

1. Personal data:

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2. Preuniversitary studies:

1978-1986 – Gymnasium School, classes I-VIII, no. 30, Craiova
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3. Universitary studies:

1991 – 1997 – University of Medicine and Pharmacy from Craiova, Faculty of Medicine, Specialization: General Medicine

4. Postuniversitary studies:

1998 – 1999 – doctor in training, specialization medicine, Clinical Emergency County Hospital Craiova
1999 – 2004 – resident doctor, specialization Obstetrics – Gynecology, Clinical Emergency County Hospital Craiova
2005 – 2009 – PhD (candidate for a doctor’s degree), University of Medicine and Pharmacy from Craiova, the base field: Medicine, specialization: Dermatology.

5. Main Specialization: General Medicine

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6. Personal Experience:

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7. Postgraduate courses:

- 30.06.2000 - 29.07.2000 – Medical Informatics Course, organized by the College of Physicians from Dolj, Craiova.
- 5.02.2002 - 15.02.2002 – The last discoveries regarding the etiology and diagnosis of sexually transmitted viral diseases, University of Medicine and Pharmacy from Craiova.
- 15.03.2002 - 30.03.2002 – Ecography: the last discoveries from obstetrical pathology, University of Medicine and Pharmacy from Craiova.
- 1.11.2005 - 1.02.2006 – Course for General and Special Ecography, UMF Craiova.
- 3.03.2006 - 19.05.2006 – Trening course for the ones who work in the DRG system (Diagnosis Related Groups), course organised by Medical College Dolj, Craiova.
- 17.04.2007 - 23.04.2007 – The last discoveries regarding the diagnosis and treatment for infections to older people, organised by UMF Craiova.

8. International and national congresses and conferences; scientific reunions:

- The symposium ‘Neuropaty and diabetical leg’, April 21, 2000, Craiova.
- The meeting of Romanian Society of Ultrasonogrpby in Medicine and Biology, the Oltenia Subsidiary, March 28, 2006, the College of Phisicians, Dolj, Craiova.
The Scientific Symposium: ‘Non-alcoholic hepatic steatosis’ organised by the College of Physicians from Olt County, April 25 2007, Slatina.


The Scientific Symposium with international participation:’ Some curative-preventive activities carried in the last 45 years’ organised by UMF Craiova, June 22-23 2007, Craiova.


9. Scientific works:

5. ‘Herpes gestationis, Case Description.’, Ştefania Dobre, Ion Ţolea, the Volume of summaries of the XV-th Obstetrics and Gynecology Congress with international participation, Bucharest 28-30 october, 2010, page 190.

10. Membership in scientific and professional societies:

1. Member of The College of Physicians Olt;
2. Member of Obstetrics and Gynecology Romanian Society;
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