

CANDIDIASIS IN PREGNANCY- PERSONAL STUDY

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Abstract. The impact of an intensive educational program regarding candidiasis in pregnancy on health professionals knowledge at Clinical Hospital of Obstetrics and Gynecology "Elena Doamna" in Iași, Romania. The study was designed in three phases: Assessment phase, Implementation phase and Evaluation phase. The study was conducted from early January to the end of December 2019. The result of the study shows that its most frequent location is in the mouth and the vagina. The symptoms are reduced and the diagnosis is based on the clinical examination, the confirmation being performed by microscopic examination. Prophylactic treatment of candidiasis involves maintaining a rigorous hygiene, avoiding excessive and unprotected use of antibiotics and increasing the body's immunity through a balanced diet and through the intake of mineral salts and vitamins.

INTRODUCTION

Candidiasis is a fungal infection that develops in conditions of appropriate temperature, moisture and environment and it can be located in the mucosa, especially in the mouth and vagina, but also in some other internal organs like the esophagus and the intestine. Its proliferation occurs when this balance is broken because of an uncontrolled consumption of antibiotics and also in case of decreased immunity (9).

After birth you can also locate it in breasts - areola and lactiferous ducts- but there is no causal link between the mother's candidiasis and that of the newborn. Symptoms consist of an appearance of white spots on the oral mucosa (muguet) with an underlying congestive background, painful itch, sometimes feeling like a burning in the breast or in the pharynx or esophagus, depending on location, or difficulty swallowing (2). In oral form, the dentist must differentiate it from other oral lesions with carcinogenic potential (leukoplakia, erythroplakia). The definitive diagnosis is made after scraping and cultivation on the Sabouraud agar, by visualizing the micelles under the microscope (5). Prophylactic therapy refers to the introduction of measures designed to control its excessive development and increase the body's immunity- rigorous oral hygiene, avoid excessive use of antibiotics and proper nutrition. Curative therapy can be performed in two ways:

- local topics – creams, shampoos, mouth water, gentian violet,
- general systemic therapy with various antifungal agents – Ketoconazole, Fluconazole, administered by mouth or parenterally. Ketoconazole and especially Fluconazole are very active on *Candida albicans*, but they also have side effects that, even if minor, should be avoided in pregnant women. They are mainly administered post-partum.

Of the fungal infections that are of interest to the pregnant woman, the most common is candidiasis, which may affect the oral cavity (muguet) (fig.1A), but also the vagina, skin, nipple, galactophore channels (lactiferous ducts). In some cases, internal organs such as the esophagus and intestine may be affected by this disease. Candidiasis is produced by a fungus called *Candida albicans* and more rarely by other strains (*Candida glabratis*, *Candida drusei* or *Candida tropicalis*). This fungus is found in healthy organisms, being part of the bacterial and fungal flora that lives in symbiosis with other microorganisms (5).



Fig.1. A. Extensive muguet, B. Glossy candidosis, C. Candida soft palate and glottis (personal collection)

The highest density of fungi develops in the oral cavity and intestines, but the saprophytic microbial flora stops their proliferation. There are certain risk factors in its occurrence and development, such as: hormonal changes during pregnancy, dehydration, diabetes, overuse of oral contraceptives, overuse of antibiotics and corticosteroids or allergic conditions (7, 10). At the buccal level the candidiasis looks like whitish spots located in the lingual, palatal, gingival areas (fig. 1 B,C) which after scraping leaves the place of a rosy and painful placard.

Sometimes they are asymptomatic, but most often they cause pain and modify taste. Oral candidiasis is considered an early sign of an alteration of the immune system, and those who present more than 200 CD4⁺ cells and who also have muguet must undergo preventive treatment against PPC (pneumonia with *Pneumocystis carinii*). Esophageal candidiasis can cause difficulty swallowing, sore throat and sometimes pain and heartburn (10).

PURPOSE AND OBJECTIVES

Through this original publication, we tried to highlight the exaggerated mode of action of the *Candida albicans* fungus on the oral cavity to the pregnant woman, in the context of existing hormonal changes in pregnancy.

The study was conducted on a large group of pregnant women and postpartum period, on 499 women, precisely to highlight these exaggerated changes produced by *Candida albicans* fungus on the oral cavity.

A complex of factors were considered (age, place of origin, educational level, parity, clinical symptomatology, various pathologies associated with pregnancy, oral hygiene, nutrition, access to the dentist, administered treatment).

MATERIAL AND METHOD

Clinical examination usually places the diagnosis, but the dentist with the obstetrician must make the differential diagnosis with other oral lesions that are potentially carcinogenic (leukoplakia, erythroplasia, lichen planus). In the latter cases, the lesion does not disappear during scraping, and on microscopic examination (fig.2) after trichromic staining, the mycelial filaments do not appear.

Diagnostic tests are represented by exfoliative cytology, isolation by growing fungi on Sabouraud medium, the use of potassium hydroxide, trichromic fixation and staining and observation under a microscope. Sometimes biopsy is required for differential diagnosis (5).

The Sabouraud medium is used for isolation and cultivation of fungi (yeasts, molds and dermatophytes) from clinical trials (fig 2). Peptones from the Sabouraud environment are a source of factors supporting nitrogen growth (1). Glucose provides an energy source for the growth of microorganisms. The high glucose concentration provides an advantage for the growth of fungi (osmotically stable), while most bacteria do not tolerate high sugar. In addition, the low pH value is optimal for fungi.(1)



Fig. 2. Microscopic examination- *Candida albicans*- pharyngeal exudate, smear, growth on Sabouraud medium, magnification 200X (personal collection)

Candida albicans can be located in pregnancy or in the confinement after birth in the mammary areola and the milk ducts. Micelles need heat, moisture and darkness for development. They colonize 90% of newborns in the first hours after birth, but there is no cause-effect relationship between breast and newborn candidiasis. The cutaneous-mucosal form occurs more frequently when the skin or mucosal integrity is affected. *Candida albicans* would be harmless if there were no cracks in the mammary areola. Proper positioning of the newborn at the breast is important in the development of breast candidiasis (8).

Consultation with a nutritionist is useful for providing enough protein, carbohydrates, fats, minerals and vitamins, which are useful both for maternal health and fetal development. Unsweetened yogurt with active bacterial cultures - acidophilic lactobacillus - is a known remedy against yeast infection (4).

Curative therapy can be divided into two groups:

- a) Topical treatments: creams, shampoos, mouthwash, gentian violet, which come in direct contact with the mucosa and skin. It is a cheap therapy with no side effects.
- b) General systemic therapy by which drugs in various forms circulate in the body and which should usually be avoided during pregnancy due to side effects. They can be administered post-partum.

Topical treatment of oral candidiasis in pregnancy includes rinsing the mouth with nystatin solutions, amphotericin B or flavonoid alcohol solution extracted from plants.

Lingual or gum swabs can also be performed with boro-glycerine, the dose and duration depending on the location and severity of the infection. A modern treatment used in candidiasis for pregnant women is Lapachol (fig. 3) an extract from subtropical plants with strong anti-fungal properties. It is used as an infusion with which you have to rinse the mouth 2-3 times a day for 14 days. Per capita consumption of pharmaceuticals during pregnancy should be avoided (6).



Fig. 3. Lapachol plant (personal collection)

Another inexpensive and handy remedy is the use of acidophilic lactobacillus, a beneficial bacterium found in the vaginal and intestinal flora, maintaining the balance of bacterial flora. It is effective for restoring intestinal flora after antibiotic therapy in particular and promotes healing mouth sores, herpes and muguet's. It is found in dairy products - yogurt,

kefir, buttermilk, but it can also be found in pharmacies as capsules or tablets, their use being indicated after oral antibiotics. Side effects are minor (bloating), and contraindication is lactose intolerance (4).

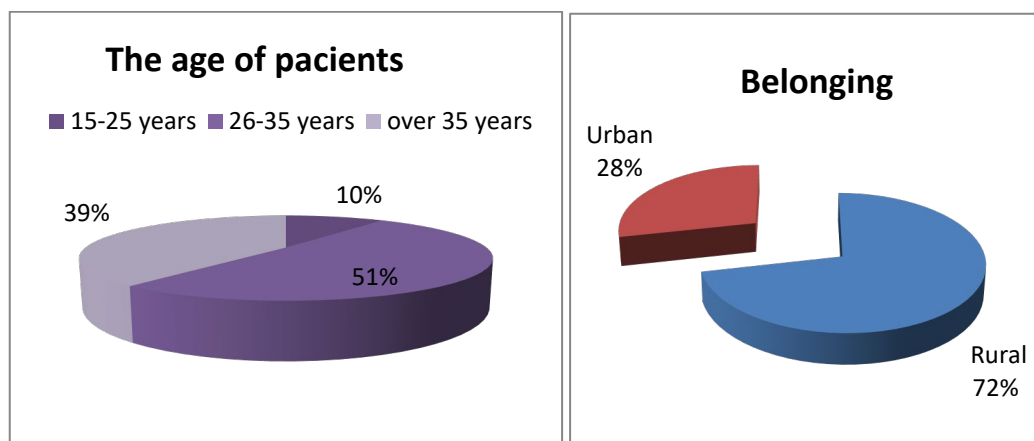
The treatment of post-partum mammary candidiasis is especially topical through the gentian violet bathing, which has immediate action and has no side effects. If the symptoms recur, the diagnosis of candidiasis is confirmed and can be continued with targeted antifungal therapy (Ketoconazole, Fluconazole).

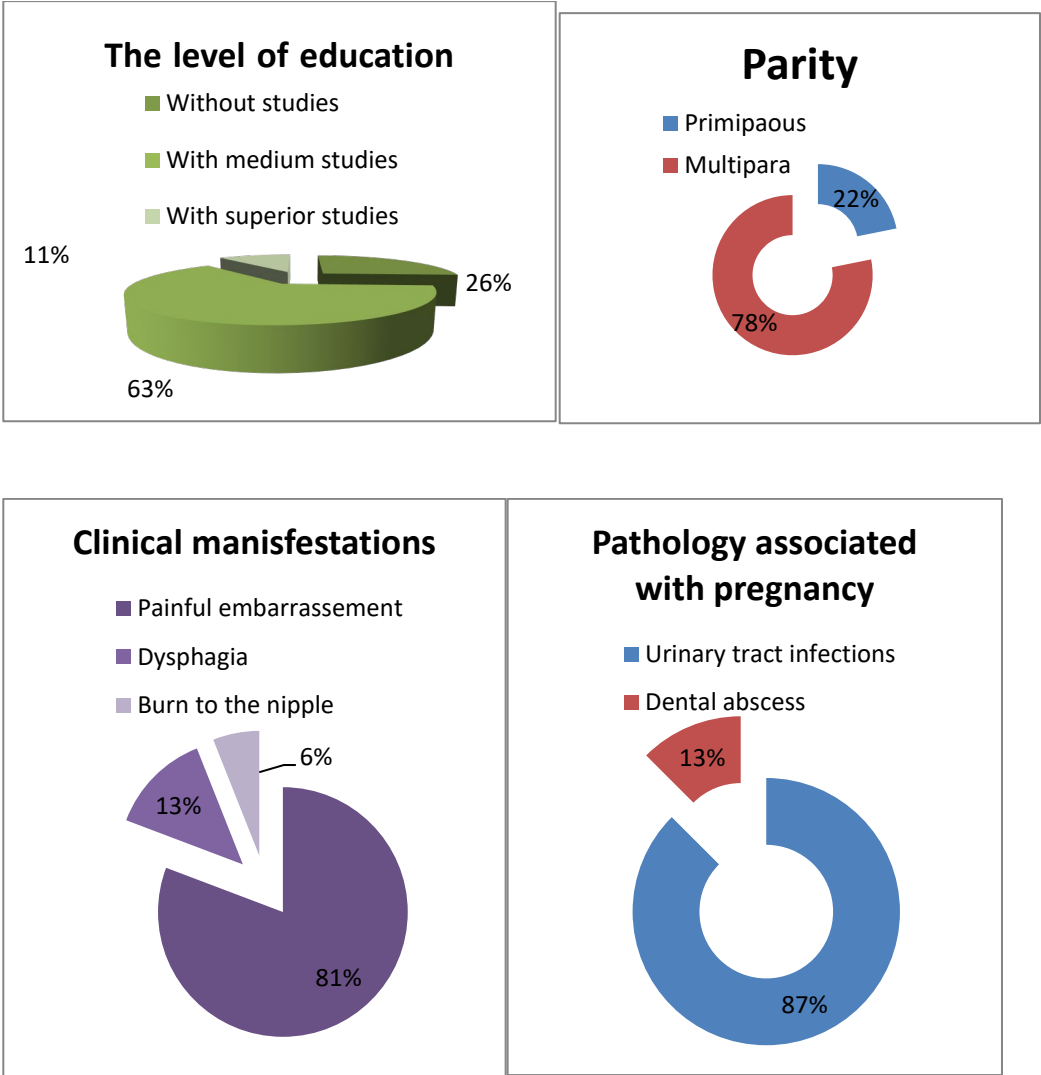
Fluconazole is an orally or parenterally administered systemic antifungal that stops candida multiplication without destroying it, which implies a long-term treatment to prevent relapses. It is well tolerated, but it also has digestive side effects (nausea, abdominal pain, diarrhea, skin rash). As it passes into milk, it is also effective in treating candidiasis of milk ducts (8).

It has no side effects on the newborn, so the mother treated with this product can breastfeed without risk. The dosage is 200 mg for the first time, then 100 mg twice a day for 14 days. In order to avoid relapses, treatment should be continued for 7 more days after symptom remission. It is good to treat the newborn as well, in which case the dose is 6 mg/kg body / day, followed by 3 mg/kg body/day for 14 days or for the whole time of the maternal therapy (11).

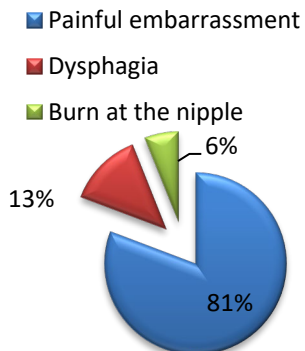
Personal study

The study was made over a period of 1 year (2019), at the Obstetrics and Gynecology Hospital "Elena Doamna", Iasi, to provide a better view on the incidence and influence of candidosis in pregnant women (375 patients) and women who gave birth (124 patients). These were divided according to the following factors: the age, belonging, educational level, parity, clinical manifestations, pathology associated with pregnancy, level of oral hygiene, consumption of dairy products, dispensary to the dentist, local treatment administered.

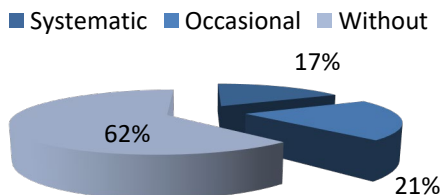




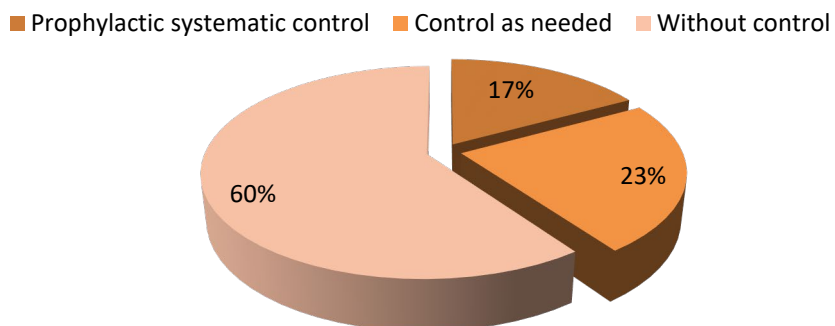
Clinical manifestations

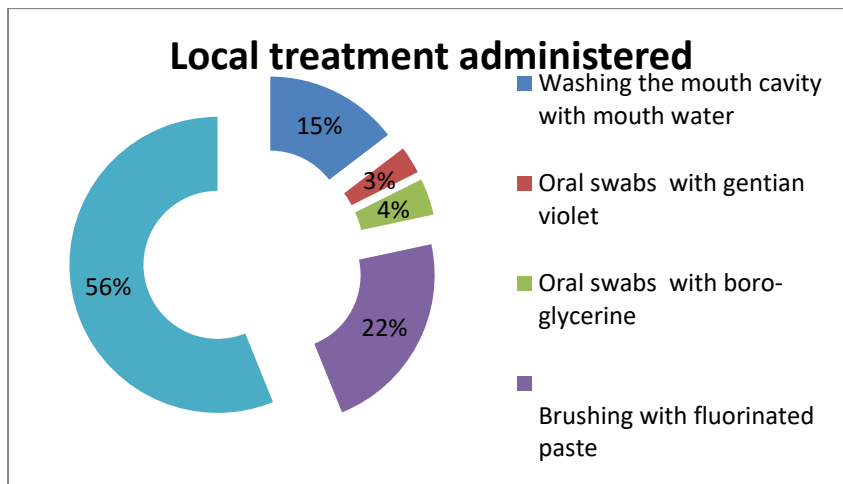


Consumption of dairy products



Dispensary to the dentist





DISCUSSIONS

From the personal study which was carried out on the 499 pregnant women and postpartum period in which the fungus *Candida albicans* manifested itself in the oral cavity we note:

- the increased number of patients aged between 26-35 years, mostly from the rural area, with medium education, multi-pair (multiple births) and low hygiene.
- the most common clinical manifestation in the studied group is represented by the painful embarrassment that appeared at the oral cavity level.
- from the 499 patients studied, a total of 120 patients had pregnancy-related pathology, of which 105 patients (87%) were diagnosed with urinary tract infection, and 15 patients (13%) with dental pathology (dental abscess), the 120 patients requiring antibiotic therapy, exacerbating element for the development of oral candidosis.
- the most patients did not consume dairy products during pregnancy (lactobacil acidophil), the dispensary to the dentist did not exist, as a result they did not receive specialized treatment.

CONCLUSIONS

Candidiasis is a fungal infection caused by a fungus called *Candida Albicans* with different location - mucous membranes, skin, and internal organs.

The causal agent lives in the human body as saprophyte, in balance with other bacteria and exacerbates its activity in case of breaking this balance by hormonal changes, excessive use of oral antibiotics and corticosteroids, as in the case of conditions that reduce the body's immunity, such as diabetes, allergic conditions.

The pathogen exacerbates its development and virulence under favorable conditions of humidity, heat, darkness and by decreasing the immunity of the host organism.

Its most frequent location is in the mouth and the vagina. The symptoms are reduced and the diagnosis is based on the clinical examination, the confirmation being performed by microscopic examination.

Prophylactic treatment involves maintaining a rigorous hygiene, avoiding excessive and unprotected use of antibiotics and increasing the body's immunity through a balanced diet and through the intake of mineral salts and vitamins.

The curative treatment can be local, using creams, shampoos, mouth water, gentian violet, boro-glycerin, or general, using oral or parenteral Lapachol, Ketoconazole and more recently Fluconazole. The latter are not given to pregnant women because of the side effects.

REFERENCES

1. Ajello, L., L.K. Georg, W. Kaplan, and L. Kaufman. 1963. CDC laboratory manual for medical mycology. PHS Publication No. 994, U.S. Government Printing Office, Washington, D.C.

2. **Esther J., Rebeca A., Nivia C., Maria M., Pilar S., Leonides F., Juan M. R.** (2017); Mammary candidiasis: A medical condition without scientific evidence?
3. **Guillermo Q., Sandra G-A., Cristina M.-A., Elena S., Estibaliz M., Nerea J., Elena E.** (2019). Therapeutic tools for oral candidiasis: Current and new antifungal drugs, *Med Oral Patol Oral Cir Bucal*. 24(2): e172–e180.
4. **Haihong H., Daniel J. M., Cuiwei W., Pilar R. H., Mandy L. B., Hui C., Richard A. C., Dongmei L.** (2014), Impact of Eating Probiotic Yogurt on Colonization by *Candida* Species of the Oral and Vaginal Mucosa in HIV-Infected and HIV-Uninfected Women, Published in final edited form as: *Mycopathologia*. 176(0): 175–181
5. **Laura C.-C., Yolanda J.-S.** (2013), Clinical and microbiological diagnosis of oral candidiasis, *J Clin Exp Dent.*, 5(5): e279–e286.
6. **Marina A. S., Susana J., Luciana A. R. dos S. L., Fernanda F. C., Isolda C. M., Heloisa B., Elaine M. de S-F., Patrícia S. C., Carlos A. R., Tânia M. de A. A., Nívea P. de S., Carlos L. Z.** (2013) The antimicrobial activity of lapachol and its thiosemicarbazone and semicarbazone derivatives, *Mem Inst Oswaldo Cruz*, 108(3): 342–351.
7. **Nahed G., Ali E.R., Ghassan G., José-Noel I.** (2019), Emergence of Vulvovaginal Candidiasis among Lebanese Pregnant Women: Prevalence, Risk Factors, and Species Distribution, *Infect Dis Obstet Gynecol*.
8. **Nikou, S.A., Kichik, N., Brown, R., et al.** (2019). *Candida albicans* interactions with mucosal surfaces during health and disease. *Pathogens* , 8: 53.
9. **Pappas PG, Kauffman CA, Andes DR, Clark CJ, Marr KA, Ostrosky-Zeichner L, et al.** (2016) Clinical practice guideline for the management of candidiasis: 2016 update by the Infectious Diseases Society of America, *Clin Infect Dis*. 62(4): e1–e50.
10. **Shankargouda P., Roopa S. R., Barnali M., Sukumaran A.** (2015) Clinical Appearance of Oral Candida Infection and Therapeutic Strategies, *Front Microbiol.*, 6: 1391.
11. **Yusuf C. K., Gideon K., Pina B.** (2015). Fluconazole exposure during pregnancy, *Can Fam Physician*. 61(8): 685–686.

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