Bulletin of the *Transilvania* University of Braşov
Series VI: Medical Sciences • Vol. 6 (55) No. 1 - 2013

POSTPONEMENT OF PREGNANCIES IN WOMEN WITH TUBERCULOSIS

M. MOGA[1] N. BÂGIU[1] A. PASCU[1]
O. DIMIENESCU[1]

Abstract: *The importance of tuberculosis (TB) occur on the fact that this disease is the mainspring of death in women all over the world. The increasing of the population number, the epidemic with HIV, raising of poverty and increasing drug resistance will affect the disease in female gender, because this group population is at risk of progression of the disease in the fertile years. The purpose of the article is to review the literature concerning the contraceptive methods that are used to avoid pregnancies at women with tuberculosis infection, the main subjects being the social, economic and medical factors that are blocking the access to medical care, also the implications and the negative effects of the disease in pregnancy and post-partum period. Postponing pregnancies at this type of patients is important because of the serious consequences of the infection during pregnancy, delivery and post-partum.*

Key words: *tuberculosis, reproductive age, pregnancy, post-partum, birth control methods.*

1. Introduction

The morbidity of tuberculosis during pregnancy is increasing all over the world, mostly in developing countries [32]. Holmes showed that in some regions of the world, the mortality of women because of active tuberculosis is higher than men23. The data show us that the most important cause of deceases among women of reproductive age is tuberculosis, accounting for 9% of female deaths worldwide [40].

Women are mostly affected by this disease during their genital active life (15-49 years), this period encompassing also the pregnancy and the post-partum – puerperium. In the terms of reproductive health, the impact of tuberculosis on women includes the consequences of the infection during fertility, pregnancy, delivery and post-partum period.

Tuberculosis per se doesn't have an unfavorable influence upon the pregnancy status and process. Untreated, tuberculosis could have a bad evolution during pregnancy period, sometimes a bad fast tracking one. The critical moments of the tuberculosis during pregnancy are: the first trimester of pregnancy and the postpartum period.

Because of the serious consequences on the health system in women with tuberculosis is important to postpone the pregnancies at least after the anti-tuberculosis treatment is instituted and has

[1] *Transilvania* University of Braşov, Faculty of Medicine.

efficacy. Regarding to the influence of pregnancy on pulmonary tuberculosis (with which the obstetrician is brought face to face) the most significant is the devastating influence of labor and the puerperium on the course of the disease.

2. Tuberculosis at women -social, economic and medical factors

The influence of tuberculosis on the maternal health is very important, especially in developing countries, where the effect of tuberculosis in pregnancy is underestimated. The nutritional status, chronicle disease like tuberculosis and pregnancy are influenced by the education, income, religious concepts, demographic features and access to medical care, all of this making part of the socioeconomic area.

Tuberculosis is known to be the disease of poverty, affecting the vulnerable groups of the world's population. Other factors like low income countries, malnutrition and food insecurity, can contribute to the deterioration of the organism, other important factors being smoking or comorbidities such as diabetes [16].

This situation appears in the context of food restriction, poverty and handicaps, being usually found in specific areas of the world, and also in ethnic minorities [15].

The weakness of female gender with tuberculosis appears from different factors that include lower awareness of the disease, lack of financial independence, and greater constraints in accessing health care services [11], [25]. Another important weak point is the association with HIV, because the HIV epidemic affects more women than men, therefore the women mortality is higher.

In HIV patients it appears a process named immune restitution when associated with tuberculosis because of the immune depression is accomplished with a redeeming of the number of lymphocyte [39]. Besides this mechanism, it was found also a paradoxical deterioration [7] to the patients treated by tuberculostatic therapy for tuberculosis and HIV negative tested.

3. Implications of tuberculosis during pregnancy and post-partum period

The clinical forms of the tuberculosis infection during pregnancy are the same like in non-pregnant women [17], the main problem being the delay in diagnosis because of the symptoms that are not specifically [14] and also because pregnancy symptoms like malaise and fatigue are often present [21].

In pregnant women, tuberculosis often starts in the acute form. In this period of the disease it can appear the infiltrative forms, along with necrogenic and bacterial excretion, frequently compound with pleurisy that is exudative, and also lesions at the level of trachea, larynx and bronchi.

The typical site in pregnancy is pulmonary tuberculosis. *Good et al* [17] pointed out in a study made on 27 pregnant women with positive culture for the disease, that cough was found in 74%, weight loss in 41%, 30% had fever, malaise or fatigue, and 19% had hemoptysis, 20% were asymptomatic but all had abnormal pulmonary x-rays [5].

Another form of this disease is the extra pulmonary localization, the incidence of this type being studied by *Wilson et al.* [42]. In their study lot 10% of pregnant women with tuberculosis were reported to have this form of the disease.

From the other perspective, pregnancy can be seen like an immunosuppressive mechanism. This phenomenon intends to avoid the natural rejection of the fetus. It appears a decreasing of lymphocytes activity that is shown by the intradermal reaction with tuberculin, as a negative response. In the childbed, after 24 hours

after delivery is expected a rebound of lymphocytic activity [12].

In the organism of a pregnant woman we can observe also metabolic changes in the most important systems (respiratory, cardiovascular, nervous and urinary) through the modifications of the placental and fetal changes at the hormonal level [10].

Regarding the frequent consecutive pregnancies, they have a negative effect on the condition of women affected by tuberculosis. The gestational period can induce the reactivation of tuberculosis process because of the decreased immune system. The reactivation of the disease is observed in those patients that are suffering of the destructive pulmonary form, and it is caused by the severity of the affection when new modifications of the organism occur, like the pregnancy. The main mechanism in pregnancy is a lower responsiveness of immune system due to an increased activity of the reproductive hormones.

The progressive iron deficiency that can cause anemia is another serious negative condition that could appear in (approx.) half of pregnant women affected by tuberculosis, most of them in the first trimester of pregnancy. This situation changes in the second trimester, when anemia can be found at almost all of the patients.

Cheng et al. showed in a meta-analysis that 93% of post-partum tuberculosis was extra pulmonary and in 69% of cases was located in the central nervous system. Even if treatment was induced, 38% of the women died and 13.8% had functional deficits [8]. The co infection with HIV, especially in developing countries where the incidence of these two diseases is very high increased the maternal risk of disease or death [20]. In these situations it is important to make active screening and to treat preventive with isoniazid the women, in order to prevent this dramatic events [20], [29].

Therefore, due to the extremely important consequences of this disease on pregnancy and women's health is good to know that a condition of pregnancy is recommended to be delayed at least a year.

Some clinicians concluded that after delivery the rapid descent of diaphragm causes lung reexpansion , and would drag open the partially healed cavity during the last months of pregnancy , this leading to exacerbation of pulmonary tuberculosis [27].

In some reports made by *Young et al*. [47], who studied 46 patients with pulmonary tuberculosis, it was pointed out that in 58.6% of cases, depreciation in the clinical condition could be observed in puerperium. In 8 cases (17.4 %) death occurred within three months.

The importance of tuberculosis associated to pregnancy arises from the fact that in this moment the symptoms can appear like active disease. In the next period, of post-partum, an acute deterioration of preexistent clinical symptoms can occur, as well as a triggering of the tuberculosis symptoms in maximum one month after.

Therefore is important for women that are in the post-partum period to postpone another pregnancy, at least one year, until the immune system is stable and it can deal with another gestation condition.

The therapeutic abortion for the first pregnancy trimester (quarter) associated with tuberculosis is highly recommended and belongs to the management of

tuberculosis. Regarding our experience, the strongest three indications for therapeutic abortion (on the first trimester are: active-evolutionary pulmonary tuberculosis in the last 12 months, evolutionary or recently tuberculosis pleurisy and stabilized tuberculosis – if the pregnancy arises to less than 18 months from a prior fetus delivery or the women has ventilation deficiencies [30]. The pregnancy discontinuation should be taken into account too if: the disease is multidrug-resistant and disease outbreaks persist, or if the woman shows immunosuppression (like marked anemia).

The procedure is thus fully justified in the case of an undesirable pregnancy in a woman who has recently passed through a gestation ending in a turbulent puerperium. We discussed above about the medical point of view and the patient safety point of view. Of course, there are a lot of interference factors which could impair the right medical decision of abortion: ignorance, poverty and no addressability, cultural and religious beliefs, husband decision, etc.

4. Management of tuberculosis in pregnancy and fertile age

The untreated tuberculosis could seriously harm the pregnant women. There is general agreement that the management of tuberculosis during pregnancy and the postpartum period is very similar to that of other patients.

The most important thing is to avoid frequent pregnancies and the long lasting period of breastfeeding.

The active disease recommends the use of isoniazid, rifampicin, and ethambutol. They are allowed in pregnancy and carry a minimal risk of fetal abnormalities or additional side effects. The streptomycin should be avoid during pregnancy. In the postpartum period, the antituberculosis treatment continues until the course is completed. The breastfeeding is encouraged, although the therapeutically agents passes into the milk. If the mother has been treated, the baby will receive isoniazid-resistant BCG and a course of prophylactic isoniazid. The treatment of multidrug-resistant tuberculosis and HIV-tuberculosis co-infection is sensitive medical fields and requires careful and expertise clinical therapy [19].

Because of its hepatic inductive effect, Rifampicin, can reduce the effectiveness of oral contraceptive pills, as well as the implants, injectable, and emergency contraceptive pills [9], [37]. In addition, rifampicin may reduce the effectiveness of anesthetics used for sterilization (female or male) or for other purposes [41]. Women who use oral contraceptives and require rifampicin should be advised to choose another appropriate contraceptive method. It is indicated also that women who are unable to find a suitable alternative to oral contraceptives should take a higher-dose ethinyl estradiol with shortened pill-free intervals during and for four weeks after rifampicin use [9].

5. Postponing pregnancies using different contraceptive methods for women with tuberculosis

The already discussed negative impact of pregnancy effects on the tuberculosis women health status suggests us how useful and proper is the postponement of other pregnancies to such kind of women. A big percentage of all women living with tuberculosis are in their fertile years,

therefore the conception is a very important decision that they need to take, given the implications of this disease in pregnancy and post-partum period [43]. The family planning methods must be implemented in each family with tuberculosis or exposed to high risks to make / repeat the disease. Among the family planning methods, we don't recommend therapeutically abortion as an option, we – as a part of women health system workers – must do all what is needed to support the organic and psychological health status of our patients.

Basically, the idea is no pregnancy until a strong health status of the female. As a general discussion, the contraceptive options are the same for all the couples, irrespective of their tuberculosis status. Furthermore, WHO agreed that nearly all contraceptive methods are deemed to be active and safe for tuberculosis positive women [45].

Hormonal control methods. WHO articles from 2004 and 2006 [45, 46] showed that is not contraindicated to use hormonal contraception (pills, injectable, implants, patches and rings), but in case of therapy for tuberculosis with rifampicin, the women will need an extra protection because this drug may decrease the effectiveness of oral contraceptives [45, 46].

There are clinical studies that show the implications of rifampicin in the hormonal system, the fact that is decreasing the blood level of estrogen and progestin found in the oral contraceptives. However this decreasing is valuable only for the long term therapy or in prophylaxis with anti-tuberculosis drugs, because in case of short-term exposure to rifampicin the contraceptive effect is normal [2, 3, 4], [31], [35, 36].

Michaelets affirmed that the liver cytochrome p450 system is induced by the rifampicin, the consequences being an increased metabolism and also a diminution of the blood levels of oral contraceptives [28]. Only rifampicin seemed to reduce the effectiveness of oral contraceptives. However, *Dickinson BD et al*. [1], [13] showed in a readable study that more than a quarter of the women consulted for abortion or family planning were taking an oral contraceptive and an antibiotic in the same time, without any supplementary protection method.

The use of condoms like a second protecting method is recommended, for preventing unintended pregnancies and also for preventing sexually transmitted diseases like HIV [46].

Intrauterine device (IUD). In case of tuberculosis infection, another contraceptive method used are the intrauterine devices. This kind of devices is used for long term contraception, being a reversible birth control method. The IUD is a device 'T'-shaped that is inserted in the uterus. It includes cooper or progesterone.

The contraindications of this method are the women with AIDS and those who are diagnosed with pelvic tuberculosis because it can increase the symptoms and aggravate the disease. In case of tuberculosis positive women it has to be taken in evidence the fact that IUD can increase the menstrual bleeding and in consequence the risk of anemia.

Because the concept of our paper is the postponement and not the avoidance for good of the pregnancy we could talk about ***Surgical sterilization***, but only with a strong acceptance of the couple. The female sterilization is more used in the countries that are in course of developing,

most of all because of the easy and fast method of contraception against pregnancies, while in developed countries more popular are the reversible methods [38]. Anyway, the above assertion that a method of women sterilization is widely used in poor countries needs some corrective discussions but the idea goes around the effectiveness. The method will prevent unwanted pregnancies that could affect the immune system of women with tuberculosis infection [32] but this kind of birth control method will not prevent against the sexually transmitted diseases!

Another option is the male sterilization (vasectomy), but it has not been well documented its use among males [24].

Emergency contraception. In this class of birth control method are included pills (high dose hormonal contraceptive pills, levonorgestrel, mifepristone, ulipristal) and also devices that are used to prevent unwanted pregnancies (intrauterine device +/- progesterone). The mechanism of this contraception is to prevent the fertilization, the egg transportation or the nidation.

It can help to prevent unintended pregnancies, therefore is important the immediate access to this method for its maximum effectiveness. *Karanja et al.* [26] analyses in a study that for the patients that are suffering of sexual abuse, the fast access to emergency contraception is vital. Another important study made by *Graham A.* [18] showed that the emergency contraception is used by some women like a regular contraception method, which is why the familial planning is important to improve knowledge of this method. This method can be used for the women with tuberculosis to prevent the unwanted pregnancies that can cause serious consequences in the health system.

Barrier birth control methods. For unwanted pregnancies it can be also used the barrier contraception, that includes: male and female condoms, diaphragms, spermicides. The mechanisms of the method regards the prevention of entering of the sperm into the uterus and the destroy of the sperm cells. The effectiveness of this method is progressively achieved but, the Pearl index (failure index of the contraceptive method) is high. A study wanted to be complex and sustains that highly effective in protecting against pregnancy are both male and female condoms [22]! Unbearable situation, of course.

In stable couples the condoms are rarely promoted because it demands communication and negotiation. *Pullum* [34] showed that the ability of the women to influence the men's knowledge of the sexual risk and condom use is higher every year.

Dual protection. The term of dual protection represents the methods used to avoid pregnancies and also to avoid the sexually transmitted diseases [44]. One of the method mostly used in this kind of contraception are the condoms, but the use of this type of protection used alone may be affected because especially the couples that are active sexually do not want to use condoms every time, that's why the protection will decrease. The role of the family planning, most of all in the stable couples, it will be to explain the advantages of using the condoms [6].

Thereby, for women with tuberculosis that is at high risk, at which a pregnancy can affect her immune system and also can reactivate the disease, is indicated to use two contraceptive methods [45].

6. Conclusions

It is important to consider tuberculosis disease in the context of socioeconomically background, not only a medical problem. Anti-tuberculosis treatment it solves partially the complex problem, in which are involved several factors, like medical, cultural, economic and social, which need a multidimensional approach.

The access to family planning services must be provided for women with tuberculosis. Counseling the patient has to be well conducted, to provide confidentiality and accurate information.

The knowledge about tuberculosis at female gender are important because of the effects on the health system, being known that in pregnancy the capacity of the immune system is decreased, and this disease have serious consequences that can lead till death of the patient. Therefore is important to delay pregnancies as long as tuberculosis is active or under treatment, and also in the post-partum period, this being accomplished using different contraceptives methods.

As a general conclusion, all the contraceptive means are useful in an attempt to postpone a "dangerous" pregnancy status. If there are possibilities to dialogue with an awarded female, she will choose the right tailored method for her. If the multilevel approach cannot function, the elective method will be chosen by the medical worker involved in women health system and will be discussed with the couple in order to obtain the informed consent.

References

1. Archer, J.S., Archer, D.F.: *Oral contraceptive efficacity and antibiotic interaction: a myth debunked*. In: J Am Acad Dermatol 2002;46:917–23
2. Back, D.J., Breckenridge, A.M., Crawford, F.E., et al. *The effect of rifampicin on norhisterone pharmacokinetics.* In: Eur J Clin Pharmacol 1979;15:193–7.
3. Back, D.J., Breckenridge, A.M., Crawford, F.E., et al.: *The effect of rifampicin on the pharmacokinetics of ethinyl estradiol in women*. In: Contraception 1980;21(2):135–43.
4. Barditch-Crovo, P., Trapnell, C.B., Ette, E., et al.: *The effects of rifampin and rifabutin on the pharmacokinetics and pharmacodynamics of a combination oral contraceptive.* In: Clin Pharmacol Ther 1999;65(4):428–38.
5. Carter, E.J., Mates, S.: *Tuberculosis during pregnancy. The Rhode Island experience, 1987–1991*. In: Chest 1994;106: 1466–70.
6. Cates, Jr. W., Steiner, M.J.: *Dual protection against unintended pregnancy and sexually transmitted infections: what is the best contraceptive approach?* In: Sexually Transmitted Diseases 2002;29(3):168–74.
7. Cheng, V.C., Ho, P.L., Lee, R.A., Chan, K.S., Chan, K.K., Woo, P.C., Lau, S.K., Yuen, K.Y.: *Clinical spectrum of paradoxical deterioration during antituberculosis therapy in non-HIV-infected patients*. In: Eur J Clin *Microbiol Infect Dis* 2002, 21:803-809.

8. Cheng, V.C., Woo, P.C., Lau, S.K., Cheung CH, Yung RW, Yam LY, Yuen KY: *Peripartum tuberculosis as a form of immunorestitution disease*. In: Eur J Clin Microbiol Infect Dis 2003, **22:**313-317.
9. Clinical Effectiveness Committee. *Use of rifampicin and contraceptive steroids*. In: British Journal of Family Planning 24(4):169–179 (January 1999).
10. Cohen, R. C.: *Effect of Pregnancy and Parturition on Pulmonary Tuberculosis*. In: Brit. Med. y. 1943:2,775.
11. Connolly, M., Nunn, P.: *Women and tuberculosis.* In: World Health Statistic Quarterly 49(2):115–119 (1996).
12. Covelli, H.D., Wilson, R.T.: *Immunologic and medical considerations in tuberculin-sensitized pregnant patients.* In: Am J Obstet Gynecol 1978, **132:**256-259.
13. Dickinson, B.D., Altman, R.D., Nielsen, N.H., et al. *Drug interactions between oralcontraceptives and antibiotics.* In: Obstet Gynecol 2001;98:853–60.
14. Doveren, R.F.C., Block, R.: *Tuberculosis and pregnancy: a provincial study* (1990–96). In: Neth J Med 1998;52:100–6.
15. Figueroa-Munoz, J.I., Ramon-Pardo, P.: *Tuberculosis control in vulnerable groups***.** In: Bull World Health Organ 2008, 86:733-735.
16. Fischbacher, C., Bhopal, R., Patel, S., White, M., Unwin, N., Alberti, K.G.: *Anaemia in Chinese, South Asian, and European populations in Newcastle upon Tyne: cross sectional study*. In: BMJ 2001, 322**:**958-959
17. Good, J.T., Iseman, M.D., Davidson, P.T., et al.: *Tuberculosis in association with pregnancy.* In: Am J Obstet Gynecol 1981;140: 492–8.
18. Graham, A., Moore, L, Sharp, D:, et al.: *Improving teenagers' knowledge of emergency contraception: cluster randomised, controlled trial of a teacher led intervention*. In: British Medical Journal 2002; 324(7347):1179.
19. Grange, J. et al.: *Tuberculosis and pregnancy*. In: *Gender and Tuberculosis,* Diwan, V.K. et al., (eds.) Göteberg. Sweden: The Nordic School of Public Health, 1998, pp. 77–88.
20. Gupta, A., Nayak, U., Ram, M., Bhosale, R., Patil, S., Basavraj, A., Kakrani, A., Philip, S., Desai, D., Sastry, J., Bollinger, R.C.: *Postpartum tuberculosis incidence and mortality among HIV-infected women and their infants in Pune, India, 2002-2005.* In: Clin Infect Dis 2007, 45:241-249.
21. Hamadeh, M.A., Glassroth, J.: *Tuberculosis and pregnancy.* In: Chest 1992; 101:1114–20.
22. Hatcher, R.A., Trussell, J., Stewart, F., et al.: *Contraceptive Technology*, 18th revised ed. New York. Ardent Media, 2004.
23. Holmes, C.B. et al.: *A review of sex differences in the epidemiology of tuberculosis.* In: International Journal of Tuberculosis and Lung Disease 2(2): 96–104 1998.
24. Hopkins, K., Maria, B.R., Riva, K.D., et al.: *The impact of health care providers on female sterilization*. In: Social Science and Medicine 2005;61(3):541–54.
25. Hudelson, P.: *Gender differentials in tuberculosis: the role of socio-economic and cultural factors*. In: Tubercule and Lung Disease 77(5):391–400 (October 1996).

26. Karanja, L.W.: *Domestic violence Uganda*. In: Human Rights Dialogue 2003; 2(10).
27. Flamagan, P., Hensler, N.M.: *Pregnancy and tuberculosis*. In: JAMA.1959:170:783.
28. Michaelets, E.L.: *Update: clinicallysignificant cytochrome p450 drug interactions*. In: Pharmacotherapy 1998;18(1):84–112.
29. Mofenson, L.M., Laughon, B.E.*: Human immunodeficiency virus, Mycobacterium tuberculosis, and pregnancy: a deadly combination***.** In: Clin Infect Dis 2007, 45**:**250-253.
30. Moga, M. : *Obstetrica-Ginecologie* (*Obstetrics and Gynecology*). Braşov. Ed. Universităţii "Transilvania" Brasov, 2010.
31. Noche-Fink, I., Breuer, H., Reimers, D.: *Effects of rifampicin on the menstrual cycle and on estrogen excretion in patients taking oral contraceptives*. In: JAMA 1973;226(3):378.
32. Ormerod, P.: *Tuberculosis in pregnancy and the puerperium.* In: Thorax 2001, 56**:**494-499.
33. Paiva, V., Filipe, E.V., Santos, N., et al. : *The right to love: the desire for parenthood among men living with HIV*. In: Reproductive Health Matters 2003;11(22):91–100.
34. Pullum, T., Cleland, J., Shah, I.: *Consensus, power and trust in the use of family planning and condoms by couples in Eastern and Southern Africa*. Paper presented at IUSSP International Conference, Tours 18–23 July 2005.
35. Reimers, D., Jezek, A.: *The simultaneous use of rifampicin and other antitubercular agents with oral contraceptives.* In: Prax Pneumol 1971;25(5):255–62.
36. Szoka, P.R., Edgren, R.A.: *Drug interactions with oral contraceptives: compilation and analysis of an adverse experience report database*. In: Fertil Steril 1988;29(5 suppl 2):31s 38s.
37. Technical Guidance/Competence Working Group and World Health Organization/Family Planning and Population Unit. Family planning methods: *new guidance*. Population Reports Series J, No. 44 (October 1996).
38. United Nations Department of Economics and Social Affairs, Population Division. *World Contraceptive Use*. New York7UN, 2003.
39. Wendel, K.A., Alwood, K.S., Gachuhi, R., Chaisson, R.E., Bishai, W.R., Sterling, T.R.: *Paradoxical worsening of tuberculosis in HIV-infected persons*. In: Chest 2001, 120**:**193-197.
40. WHO Global Tuberculosis Program. *TB is single biggest killer of young women* (May 1998).
41. WHO. *Improving Access to Quality Care in Family Planning: Medical Eligibility Criteria for Contraceptive Use*. WHO/FRH/FPP/96.9. Geneva: WHO (1996).
42. Wilson, E.A., Thelin, T.J., Dilts, P.V.: *Tuberculosis complicated by pregnancy***.** In: Am J Obstet Gynecol 1972;115:526–9.
43. World Health Organisation; *World Health Report*; 1999, 1236.
44. World Health Organization. *Joint WHO/UNAIDS/UNFPA Policy Statement. Dual protection against unwanted pregnancy and sexually transmitted infections, including HIV.* 1 December 2000.

45. World Health Organization. *Medical Eligibility Criteria for Contraceptive* Use. 3rd ed. Geneva7 WHO, 2004.
46. World Health Organization. *Sexual and Reproductive health of Women with HIV. Guidelines on care, treatment and support for women living with HIV and their children in resource-constrained settings*. Geneva7 WHO, 2006.
47. Young, J.: *Pulmonary Tuberculosis and Pregnancy.* In: Brit. Med. J., 1936, 2. 749.