Trends of syphilis of epidemiological data, clinics and laboratory results among women in the Hospital of Lithuanian University of Health Sciences Kauno Klinikos

Kaunas
2017
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Summary

English

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Title: Trends in syphilis of epidemiological data, clinics and laboratory results among women.
Scientific supervisor: Assoc. prof. Vesta Kučinskienė

Background: Syphilis carries a significant medical burden. It has been found that the women constitute a heterogeneous group in terms of socio-economic level, health status and type of work and these factors can contribute as a risk to acquire this infection. Syphilis has three stages through which the disease can progress if the patient is not properly treated. The problem of syphilis in pregnant women is that the infection can damage not only women health but can lead to congenital syphilis (CS). The diagnosis of syphilis depends on the clinical findings and also the results of laboratory tests.

Aim: The aim is to estimate demographic data and identify clinical and laboratory peculiarities of syphilis among women.

Objectives:
1. To review demographic data among women with syphilis.
2. To analyse clinical symptoms and laboratory tests for making the diagnosis of syphilis among women treated in Kauno klinikos in 5 years (2012-2016) and compare the data with literature information.

Methods: A descriptive analysis of 17 clinical cases of women who were diagnosed with syphilis at Kauno klinikos was made. Demographic data, risk factors, the stages of the disease and the laboratory tests performed to diagnose the infection were collected from the documentation. Analysed data was compared with the information from literature review.

Results: The number of syphilis cases among women in Kaunas is low. Mainly, the women are from urban area (52.9%) and the majority of them are married (52.9%). Most of them were diagnosed during pregnancy (35.3%) due to the lack of awareness and the asymptomatic period during the beginning of the infection in the primary stage. Concomitant STDs (HIV and Candidiasis) were found in three of 17 women. The main diagnostic method to diagnose syphilis were serologic reactions (mainly RPR and TPHA).

Conclusion: In Lithuania, the incidence of syphilis among women is low. The high-risk group based on age is between 20-30 and the majority of these females come from urban area. Most of the women were diagnosed with latent or tertiary stage with cardiovascular, neurological and ophthalmologic complications. The serological testing that was performed to make diagnosis of syphilis consisted from RPR and TPHA and both tests were found to be positive during diagnosis. Most of the women repeated RPR test one year after the treatment and it was decreased 4-fold or more.

Recommendations: Promote the safe sexual behaviours among females making them more aware about the possibilities of getting a STD and its complications.
Conflicts of interest

The author reported no potential conflicts of interest with respect to the research and authorship. Author received no financial support for the research and authorship.
Acknowledgment

I am very grateful to Assoc. prof. Vesta Kučinskienė for guide me in the process of this research and to the Department of Skin and Venereal Diseases to provide me with the data information from the clinical cases of the patients.
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V k. stud. Eval Lumbrera Moreno (mokslinio darbo vadovė: prof. Vesta Kucinskiene, LSMU
KK Odos ir venerinių ligų klinika) mokslinio-tiriamojo darbo temas: „Trends in syphilis epidemiological data, clinics and laboratory results among women“ tiriamojo darbo anotacija, kuri leidžia spresti, jog planuojamame tyrimo neturėtų būti pažeistos tiriamojo teisės, todėl šiam tyrimui pritariama.

Bioetikos centro vadovas

dr. Elzėta Petušiūtė
<table>
<thead>
<tr>
<th>Abbreviation</th>
<th>Description</th>
</tr>
</thead>
<tbody>
<tr>
<td>CS</td>
<td>Congenital syphilis</td>
</tr>
<tr>
<td>CSF</td>
<td>Cerebrospinal fluid</td>
</tr>
<tr>
<td>EU/EEA</td>
<td>European Union and the European Economic area</td>
</tr>
<tr>
<td>FDUS</td>
<td>Female drug users</td>
</tr>
<tr>
<td>FTA-Abs</td>
<td>Fluorescent Treponemal antibody absorption</td>
</tr>
<tr>
<td>HIV</td>
<td>Human immunodeficiency virus</td>
</tr>
<tr>
<td>HPV</td>
<td>Human papilloma virus</td>
</tr>
<tr>
<td>MSM</td>
<td>Men who have sex with men</td>
</tr>
<tr>
<td>PT</td>
<td>Patient</td>
</tr>
<tr>
<td>RPR</td>
<td>Rapid plasma reagen</td>
</tr>
<tr>
<td>STDs</td>
<td>Sexual transmitted diseases</td>
</tr>
<tr>
<td>STIs</td>
<td>Sexual transmitted infections</td>
</tr>
<tr>
<td>SW</td>
<td>Sex workers</td>
</tr>
<tr>
<td>TPHA</td>
<td>Treponema pallidum haemaglutination assay</td>
</tr>
<tr>
<td>VDRL</td>
<td>Venereal diseases research laboratory</td>
</tr>
<tr>
<td>WHO</td>
<td>World Health Organisation</td>
</tr>
</tbody>
</table>
Terms

**Anogenital warts:** sexually transmitted disease- intraepithelial lesions caused by *human papillomavirus (HPV).*

**Candida:** species of yeast which cause fungal infection.

**Chancre:** red, round painless ulcer located at the inoculation site in a patient who has been infected by *Treponema Pallidum.*

**Chlamydia Tracomatis:** intracellular bacteria that cause the sexual transmitted infection.

**Congenital syphilis:** congenital infection caused by *Treponema pallidum.*

**Neisseria gonorrheae:** gonococcus bacteria which causes the sexual transmitted infection known as gonorrhoea.

**Non-treponemal tests:** serological tests for syphilis (e.g. RPR, VDRL) in order to detect reagin (a mixture of IgG and IgM antibodies in the sera of patients with syphilis) that is capable of reacting with complex antigen (a mixture of cardiolipin, lecithin and cholesterol) in the test [28].

**Syphilis:** sexual transmitted disease caused by *Treponema Pallidum.*

**Transgender:** refers to people who has a gender expression which differs from their assigned gender

**Treponema pallidum:** spirochaete bacterium which cause the treponemal disease such as syphilis.

**Treponemal tests:** tests which use whole cell lysates of *T. pallidum* or single or a mixture of recombinant treponemal antigens to detect antibodies against specific treponemal cellular components (e.g. TPHA, FTA-Abs). They usually remain positive for life even after provision of successful therapy [28].

**Trichomonas vaginalis:** parasite which is the causative agent of trichomoniasis
Introduction

Syphilis is a complex systemic infectious illness caused by *Treponema Pallidum*. The transmission of this disease is due to sexual contact with a person who is already infected.

Right in 21st century, despite the cause of the sexual transmitted diseases (STDs) and the manner of prevention are already known, it seems that not all the people is aware about the danger of practice sex without protection.

Syphilis is still a significant medical, economic, societal, emotional and public health load. The prevalence depends on the area, as developing countries like Africa have higher prevalence and incidence of syphilis than in America or countries of Europe [1].

The burden issue of this research is the severe aspects of this infection on females during pregnancy and after it, the epidemiology of syphilis in women, its risk factors, clinical data and diagnosis methods in women.

In 2016, the World Health Organisation (WHO) moved to a strategy to lessen the 90% incidence of syphilis and gonorrhoea from 2018 to 2030. This decision was because significant morbidity and mortality a consequence of the females who were not treated at time due to the delay of diagnosis of the infection which caused the increase rate of congenital syphilis [2]. It is estimated that in 2008 at least 1.36 million pregnant women worldwide suffered from syphilis provoking 520.905 adverse pregnancy outcomes [2].

In Lithuania, the incidence between 2014-2016 decreased from 8.8 to 5.8 cases per 100.000 population. [3]

From all cases registered in Lithuania the cases registered in Kaunas were in 2013 7.1 cases per 100 000 population, in 2014 8.0 cases per 100 000 population, 2015 10.5 cases per 100 000 population and in 2016 4.2 cases per 100 000 population. In these reported cases demonstrate that in this area, particularly, in 2015, the incidence of syphilis was especially high in Kaunas. Analysing the number of the cases depending on the sex, it was found that syphilis was more common in men than in women, respectively 87 and 64 cases in 2015 [3].

The goal is going to be obtain describing, studying and comparing the all possible cases registered in Kauno klinikos in the Department of Skin and Venereal disease. From these cases the epidemiology, demographic data, risk factors, clinical manifestations, the test performed for the diagnosis and the negative outcomes can be studied and with it it can be specify the incidence and prevalence depending on the localization, the causes of the delay in the diagnosis, the factors that can be associated to the infection and
the main laboratory tests performed to clarify the diagnosis in Kaunas 2012-2016.
Aim and objectives of the thesis

Aim

The aim of the present work is to estimate the demographic data of syphilis and identify clinical peculiarities of syphilis among women.

Objectives

1. To review the publications on epidemiology data of syphilis among women.
2. To analyse demographic data and clinical symptoms of syphilis among women treated in Kauno klinikos in ten years (2012-2016) and compare the data with literature information.
Literature review

1. Epidemiological data

1.1 Prevalence and incidence

According to WHO, every day, more than 1 million people get a sexually transmitted infection (STI). Approximately 357 million people are estimated to contract one sexually transmitted infections (STIs) annually, 5.6 million from these people are new cases of adults infected with syphilis worldwide. [6]

More than 900 000 pregnant women contracted syphilis in 2012 worldwide, causing complications in about 350 000 cases, including cases of prenatal death. [6]

In European Union and the European Economic area (EU/EEA) the incidence of syphilis in 2013 was 5.4 cases per 100 000 inhabitants. The number of the reported congenital syphilis was 65 in the same year in EU/EEA. [4] In 2015 the syphilis rate increased and there was an incidence of 6.0 cases per 100 000 population. [25]

In 2016, 151 cases of syphilis were registered in Lithuania. The incidence has decreased: from 9.7 to 5.3 cases in 2015 and 2016 respectively. In the 2016 year, the highest rates of morbidity were registered in Šiauliai, Marijampolė and Telšiai, and the lowest ones were in Panevėžys, Klaipėda and Utena. More than half of cases of syphilis (55.0%) were found in the early stage, 37.3% from these cases were women. Latent syphilis was diagnosed in nearly 29.1% of the infected. Late Syphilis was detected in 10 patients, 3 of them were women. In 2016, there were no recorded cases of congenital syphilis. [3]

Syphilis, as one of the curable STIs in the 21st century, is still an important burden issue in the health care system. A serious complication of syphilis in women, when this is not treated at time is the congenital syphilis. Although comparing both sexes, the incidence of syphilis is higher in males, with an estimated male to female ratio of 5.2:1[20], particularly in men who have sex with men (MSM) [4,9,12].

Nevertheless, the incidence of acquired syphilis in women may vary between different countries. It is known that syphilis is more common in developing countries as Zambia, Mozambique and Ethiopia than in Europe or United States of America [1].

1.2 Risk factors

Women who are more affected by Treponema pallidum include those ones who are participating in risk practices that leads to get STDs [5], as the sex workers (SW) [17,12] in particular street-based female
sex workers [14], they should be taken into account when we are talking about the risk group of syphilis.

Female drug users (FDUs) are also a high risk group. The use of synthetic drugs, known as ‘club drugs’ is usually followed by unprotected sex behaviours which leads to higher prevalence in syphilis, commonly between younger women, under 30 years old [13].

It is reported in some studies that in Asiatic countries as Thailand, Indonesia, Vietnam, where the transgender women in the population are more common, and also in America, the prevalence of syphilis is higher in these women. They also showed that transgender women who already have HIV infection constitute a significant factor associated with the acquired syphilis [7,10].

Risk factors can be classified in a variety of levels which include individual, interpersonal, community and structural factors [12]. This means that social and economic status, place of birth or residency and education are also factors that may contribute to the risk of coming down with the disease [17, 5, 13]. The number of life-time sexual partners, even the marital status, constitute a risk factor to acquire syphilis and other sexual transmitted diseases (STDs) [4].

A study in Brazil that evaluates the prevalence and factors associated with the parturient women, establish that there is an increased risk of getting STDs in women who become sexually active in younger ages due to the awareness of the vulnerability conditions, and the unstable and immature conditions and also the non-use on condoms in their relationships [27].

2. Clinical symptoms

Syphilis, at the beginning of the disease, in the early stage, can be asymptomatic in many cases. This does not mean that primary syphilis is less common but as the early stage does not manifest clearly, women seek the doctor when they already have a stage more advanced which leads them to be during a prolonged time without any treatment for the infection. The hallmark of primary syphilis is the chancre, a single red, round and painless ulcer located at the site of inoculation. This painless ulcer makes the early stage of the infection unnoticed by the patient [14, 22].

The manifestation of the secondary syphilis, in which appears the skin lesions on the palms and soles, which can make us think about any other dermatological diseases and it is easily overlooked or the tertiary stage of syphilis, which has cardiovascular and neurological involvement [16], can explain why more women seek for medical attention and they are diagnosed in the secondary, latent or tertiary stage of the infection [14,22].

What it is a really women’s health concern is the infection during pregnancy, which can lead to negative outcome of pregnancy and the mother-to-child transmission. These include low birth weight, foetal
death, miscarriage and prematurity [19].

Some studies show that untreated woman has the 70% of possibilities to get a foetal infection during the first 4 years of disease. The 35% of foetuses are born alive with congenital syphilis (CS). In fact, about 60% of new-borns are asymptomatic at birth. The risk of miscarriage and foetal infection decrease 10% in early latent stage as in some reported cases have been seen and the risk of foetal infection increase with gestational age, the manifestation of CS depend also on it and stage of maternal syphilis, treatment and immunological response of the foetus [26].

3. Laboratory data

Syphilis infection can be detected by the clinical findings and the positive results in the laboratory tests. The appropriate diagnostic techniques are vital for the control of the disease. There is a classification of the possible tests that can be performed to diagnose syphilis. The main diagnostic method is the dark-field microscopy during which treponemes can be visualized but it is less specific and sensitive. In addition, this diagnostic method is not widely available and it is complicated by the numerous saprophytic spirochetes which are present at oral and rectal mucosal surface.

Serologic tests remain the mainstay for the diagnosis of syphilis. There are two type of antibody tests: non-treponemal tests, which include Venereal Disease Research Laboratory (VDRL) and Rapid plasma reagin (RPR) test, and the treponemal tests, which include Treponema pallidum haemagglutination assay (TPHA), fluorescent treponemal antibody absorption (FTA-Abs), and other. They are used to confirm the diagnosis [16].

WHO suggest that all pregnant women, including those one who come from population with high or low prevalence of syphilis, should be assessed for syphilis in the first antenatal care visit and repeated early in the third trimester [23].

There are studies which show that women sometimes are not even aware if VDRL test was performed during their prenatal care visit, demonstrating the failure of health care services to measure, prevent and control the transmission of syphilis [27] and the lack of the information and education transmitted from the physicians to women to make them more conscious about significance of the prevention and screening of the disease.

The screening and diagnosis in early syphilis for women who are pregnant or who want get pregnant can be the best medical intervention and the most effective to prevent the negative outcomes.
Methods

A retrospective analysis was conducted on medical records of the group of syphilis-positive females (pregnant and non-pregnant females) (N=17) treated in Kauno klinikos in 2012-2016. All women had a confirmed diagnosis of syphilis according to the case definitions, which are in accordance with the EU/EEA case definition.

Demographic data, risk factors and diagnostic methods were collected from the documentation at the Department of Skin and Venereal Diseases in Kauno klinikos. For demographic data of these patients, the following variables were analysed: age, residency (rural vs. urban), marital status and employment status. For the risk factors, the variables such as the number of life-time sexual partners, source of contact (causal vs. steady partner), concomitant STDs (HIV, Chlamydia trachomatis infection, Candida, Trichomonas vaginalis, Neisseria gonorrhoeae infections, anogenital warts), number of pregnancies and previous congenital anomalies in the foetus were analysed. Finally, the following diagnostic methods were analysed to know what type of methods were performed to diagnose the disease: Rapid plasma reagen (RPR) before and after the treatment, Venereal Disease Research Laboratory (VDRL), Hemagglutination-T. pallidum (TPHA), For statistical analysis, Student t-test and $\chi^2$-square was used and the level of significance was set at $\alpha=0.05$.

Ethical aspects

This research and the collection of data from the medical records was approved by the Bioethical Center from the Lithuanian University of Health Sciences, Faculty of Medicine.
Results

1. Demographic data

In the period between 2012-2016, 17 females were diagnosed and afterwards treated due to syphilis infection in Kauno klinikos. Among these women 6 (35.3%) were pregnant and 11(64.7%) were non-pregnant.

The interval of age of these women is 23-67 years old. Pregnant females were within the range of 23-44 years old.

In the Table 1, demographic data collected from the clinical cases of these patients are shown. From these 17 women 8 (47.1%) were from rural area and 9 (52.9%) from urban area. It also demonstrates that pregnant women were younger and the most of them were single and from rural area. Non-pregnant females show a group of older women with a majority of married and from urban area. Just one of them was divorced. There were no statistically significant differences between pregnant and non-pregnant women.

<table>
<thead>
<tr>
<th>Table 1. Demographic data of women with syphilis</th>
</tr>
</thead>
<tbody>
<tr>
<td>Pregnan</td>
</tr>
<tr>
<td>t women</td>
</tr>
<tr>
<td>x±σ</td>
</tr>
<tr>
<td>Range</td>
</tr>
<tr>
<td>Residency</td>
</tr>
<tr>
<td></td>
</tr>
<tr>
<td>Marital status</td>
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<td></td>
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<td></td>
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<tr>
<td></td>
</tr>
</tbody>
</table>

Analysing the documentation was complicated to find the employment status for all the patient just two of them were documented as workers, a cashier, who was pregnant, and a cooker. Four of them did not work at that moment and for the rest of the patients, which represent 64.7%, the employment status was not found. None of these females are involved in any commercial sex work.
2. Risk factors

For this point, the possible causes and factors that can increase the risk to get the infection were evaluated. Although not all the variables that can be associated with the disease were possible to get from the documentation. The history of blood transfusion, congenital anomalies in the foetus previously and the possibility that the women could be drug users were three factors that could not be found in the documentation of all patients.

One third (5/17) of women admitted that the possible source of syphilis was a casual contact, one of them was diagnosed during pregnancy. For more than half of females (64.7%), it was difficult to clarify the source of contact from where they got the STD.

In general, these women confess to have had at least 2 sexual partners during their life. Exactly, 5 (29.4%) women had 2 sexual partner and only 1(5.8%) confess have had just one sexual partner in her whole life.

In the table 2, the concomitant STDs were examined, 2 of the pregnant woman had positive test for HIV and candida and just one from non-pregnant women had positive test for candida.

Table 2. Concomitant STIs

<table>
<thead>
<tr>
<th></th>
<th>Pregnant women N=6</th>
<th>Non-pregnant women N=11</th>
<th>P value X²</th>
</tr>
</thead>
<tbody>
<tr>
<td>HIV</td>
<td>1(16.7%)</td>
<td>0</td>
<td></td>
</tr>
<tr>
<td>Chlamydia trachomatis</td>
<td>0</td>
<td>0</td>
<td></td>
</tr>
<tr>
<td>Candida</td>
<td>1(16.7%)</td>
<td>1(9.1%)</td>
<td>0.317</td>
</tr>
<tr>
<td>Trichomonas vaginalis</td>
<td>0</td>
<td>0</td>
<td></td>
</tr>
<tr>
<td>Anogenital warts</td>
<td>0</td>
<td>0</td>
<td></td>
</tr>
<tr>
<td>Neisseria gonorrhoeae</td>
<td>0</td>
<td>0</td>
<td></td>
</tr>
</tbody>
</table>

Pregnant females had around 1-2 pregnancies and just 1 of them had 8 pregnancies. Two non-pregnant women had 3 pregnancies and the other 2 had 4 and there is one female from this group who had just 1 pregnancy.
Table 3. Number of pregnancies

<table>
<thead>
<tr>
<th></th>
<th>Pregnant women N=6</th>
<th>Non-pregnant women N=11</th>
<th>P value</th>
</tr>
</thead>
<tbody>
<tr>
<td>1-2 pregnancies</td>
<td>5</td>
<td>1</td>
<td>0.023</td>
</tr>
<tr>
<td>3-4 pregnancies</td>
<td>-</td>
<td>4</td>
<td>ns</td>
</tr>
<tr>
<td>5-6 pregnancies</td>
<td>-</td>
<td>-</td>
<td>ns</td>
</tr>
<tr>
<td>7-8 pregnancies</td>
<td>1</td>
<td>-</td>
<td>ns</td>
</tr>
</tbody>
</table>

Among the women who have declared to have been pregnant previously, some of them admit have had prematurity birth and miscarriages.

3. Clinical data

The majority of these patients (47.1%, n=8), were diagnosed at latent stage. The 41.2%, (n=7) females, were diagnosed at tertiary stage: 2 (28.6%) of them had cardiosyphilis, 4 (57.1%) had neurosyphilis and 1 (14.3%) with oculosyphilis. Most of the pregnant women were diagnosed at latent stage and non-pregnant women at tertiary stage.

Table 4. Stages of syphilis in women at the time of the diagnosis

<table>
<thead>
<tr>
<th>Stages of Syphilis</th>
<th>Pregnant women N=6</th>
<th>Non-pregnant women N=11</th>
<th>P value X²</th>
</tr>
</thead>
<tbody>
<tr>
<td>Primary stage</td>
<td>0</td>
<td>0</td>
<td></td>
</tr>
<tr>
<td>Secondary stage</td>
<td>1 (16.7%)</td>
<td>1 (9.1%)</td>
<td>0.037</td>
</tr>
<tr>
<td>Latent stage</td>
<td>5 (83.3%)</td>
<td>3 (27.3%)</td>
<td></td>
</tr>
<tr>
<td>Tertiary stage</td>
<td>0</td>
<td>7 (63.6%)</td>
<td></td>
</tr>
</tbody>
</table>
4. Diagnostic methods

Most of these women were diagnosed at the time of one of their pregnancies during the screening by performing serological tests. The diagnosis laboratory methods, were serological reactions RPR and TPHA, for neurosyphilis VDRL-CSF and TPHA, also radiological tests for tertiary syphilis.

Non-treponemal test RPR before treatment for all the women (100%) was positive. RPR after one year from the start of treatment, 12 (70.59%) were positive, 1 (5.88%) was negative and for 4 (23.53%) of them the results are not known.

Seven (58.33%) patients (PT) from these positive results in RPR after the treatment showed a response to treatment decreasing 4-fold if the titre even more in some of them (PT2 1:128-1:16; PT5 1:16-1:8; PT7 1:64-1:16; PT9 1:16-1:4; PT12 1:4-1:2; PT14 1:64-1:8; PT17 1:16-1:2).

Treponemal test TPHA test which is used to confirm the diagnosis of syphilis all the women had positive getting most of them (88.2%) +4 in the results.

The VDRL-CSF reaction was performed for just for 6 patients, 3 of them were positive.

---

**Table 5. Non-treponemal serological data**

<table>
<thead>
<tr>
<th>RPR</th>
<th>Pregnant women</th>
<th>Non-pregnant women</th>
<th>P value</th>
</tr>
</thead>
<tbody>
<tr>
<td>≤ 1:16</td>
<td>N=6</td>
<td>N=11</td>
<td>X²</td>
</tr>
<tr>
<td></td>
<td>6(100%)</td>
<td>7(63.6%)</td>
<td>0.91</td>
</tr>
<tr>
<td>&gt; 1:16</td>
<td>0</td>
<td>4(36.4%)</td>
<td></td>
</tr>
</tbody>
</table>

**Table 6. Treponemal serological data**

<table>
<thead>
<tr>
<th>TPHA</th>
<th>Pregnant women</th>
<th>Non-pregnant women</th>
<th>P value</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>N=6</td>
<td>N=11</td>
<td>X²</td>
</tr>
<tr>
<td>+1</td>
<td>0</td>
<td>0</td>
<td></td>
</tr>
<tr>
<td>+2</td>
<td>0</td>
<td>0</td>
<td>0.643</td>
</tr>
<tr>
<td>+3</td>
<td>1(16.7%)</td>
<td>1(9.1%)</td>
<td></td>
</tr>
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<td>+4</td>
<td>5(83.3%)</td>
<td>10(90.9%)</td>
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Discussion of the results

This research was focused on women to demonstrate the syphilis burden among them, seeing the importance of the early diagnosis to avoid the possible consequence or sequelae of a late diagnosis which could lead to increase the risk of congenital syphilis because of the mother-to-child transmission.

1. Incidence and demographic data

Worldwide, the number of new cases of adult people who get syphilis is 5.6 million each year [6]. Compared to women, normally the cases of syphilis in men are more frequent especially MSM [4,20]. Although women signify an important burden for the health system due to the negative outcomes that can be caused by a delay diagnose of the infection and their consequences [4].

In Lithuania, the epidemiological data demonstrate that the incidence of syphilis in the whole country between 2015 and 2016 decreased from 9.7 to 5.3 cases having the highest morbidity rates in Šiauliai, Marijampolė and Telšiai and the lowest in Panevėžys, Klaipėda and Utena. Thus, it can be affirmed that the incidence varies significantly with the geographic location [3].

Most of these women (52.9%) from this research come from urban area while the females from rural area represents 47.1% of cases, so it can be concluded that women who originate from urban area where the population is highest (299.601 in 2015) and the possibilities of knowing a number of more people and have more casual contact can contribute and being a risk factor for getting the disease.

2. Age and employment status as a risk factor

In our research the median of age of these females was for pregnant women 30.8 and for non-pregnant women 47.7, the youngest was 23 years old and the older one 67. From all these 17 patients the majority group of age is between 20-30 years which means that the younger women have a greater risk to get this STD as it was demonstrate in a study in Brazil in which said that girls with a younger age to become sexual active have more risk to get venereal diseases [27], also probably due to the lack of consciousness about the problem that can be caused due to unprotected sex with casual partners and the danger that comes with it.

The greater risk of getting this disease is for those persons who work in jobs where their bodies are exposed to the danger of different STIs and there is not so much control on the protection or the economic possibilities for this are low [5,14]. Less developed countries Mozambique, Zambia and Ethiopia
exemplifying this type of situation where the knowledge about the STDs how it spreads and the methods to avoid are still sanity problem which is not resolved [1]. The WHO estimate a 10% ascending prevalence for high risk-group of females comparing it with the low-risk groups [2]. The sex workers, MSM and transgender women constitute a high risk group [10,12]. The concept about transsexuality is more seen in countries such as Indonesia, Vietnam or Thailand [7] but not Lithuania. To examine this point, the employment status of the patients was collected but in some of the documentation their work was not specified.

3. **Source of contact**

The number of partners during their life or the number the different sexual contacts theoretically can be directly proportional to the STIs that a person can get during his life [4]. This can explain also why FDUs and SW are within the high-risk group for venereal disease [12,13].

In this research the information about number of sexual contacts or partners was collected as well as the possible type of contact (steady vs. casual) and the marital status. For those cases from where we could clarify the number of sexual partners most of them admit to not be monogamous. Although the most part of them declare to be married (52.9%), some of them affirm to live with another man who is not their husband. Only one of all their husband was positive for syphilis infection.

All this data corroborates that casual sex or more different sex partners increase the risk to get syphilis or another STD.

4. **Concomitant STDs**

HIV is an associated viral infection to syphilis infection [7]. For this reason, other sexual transmitted diseases like Candidiasis, Anogenital warts, Gonorrhoea, Trichomoniasis, *Chlamydia trachomatis* and HIV which can also associated with syphilis infection [4] were investigated in these patients to look for a correlation between getting syphilis and getting also other STDs during their life.

A study in Poland showed that 24% of females had Candidiasis at the same time that syphilis was diagnosed demonstrating the pathogen *Candida* like the most frequent concomitant disease [4].

In Kauno klinikos, 5.9% (n=1) of women were infected by HIV and the 11.8% (n=2) infected by *Candida*. This means that at least in one fifth of these women can exist an association between the infection of syphilis and the infection of the concomitant STDs, they maybe got it from the same person or due to the
causal sex because one of them admit that the possible source of infection was a casual partner or the number of sexual partners or even the non-use of condom in their relationship.

5. Pregnancy and possible outcomes

Syphilis can lead to mother-to-child transmission that can give rise to adverse negative outcomes of the foetus like foetal loss, prematurity, low birth weight, neonatal or infant death and congenital syphilis among new-borns [20].

In the reported cases from Kauno klinikos, six females were pregnant, one of them was diagnosed at the Obstetric department at the 25 weeks of the pregnancy. It is known that there were two prematurity birth and two miscarriages when they already had the infection.

The rest of patients did not report any adverse negative outcomes during their delivery or about the health of the foetus in the documentation.

6. Stages at the time of the diagnosis

It has been reported in the official report that more than half of cases of syphilis (55%) were found in the early stage, men were 1.7 times more than women: 62.7% and 37.3% in Lithuania. Latent syphilis was diagnosed in nearly one third of the infected. Late syphilis was detected in 3 women from the 10 registered persons [3].

In Poland, it was estimated that almost all women were diagnosed at early latent stage and secondary stage [4].

The main reason of the late diagnosis is the asymptomatic cases of syphilis. In the primary stage patients do not notice the first symptom (chancre) clearly as a STD. Some other females simply do not relate their symptoms with a STI because they are monogamous [14,22]. Women get the infection without knowing and past from the primary to the secondary stage.

In this research it was found that almost all the females were diagnosed at the latent stage and the tertiary stages with already some neurologic, cardiologic and ophthalmologic complications. Some of the infection was detected at the time of the prenatal screening increasing the risk for the foetus for the complication during the pregnancy.
7. Diagnostic methods

Although in the literature for the main diagnostic method is recommended the dark-field microscope for the primary syphilis diagnosis, it is not widely used because it can not differentiate *Treponema pallidum* from the other species of *Treponema*. Despite the fact that there have been a lot of efforts to try to cultivate the pathogen in vitro, this has been ineffectual. The non-treponemal tests following by the treponemal test to confirm the diagnosis are the mainstay of laboratory for the detection of syphilis infection [16].

The serological screening for syphilis during pregnancy should be done during the first antenatal visit. In regions with high prevalence or for high-risk groups the tests should also be done twice in the third trimester [16,23].

In Kauno klinikos, the principal diagnostic methods to detect syphilis are non-treponemal test RPR before and after the treatment and the treponemal test TPHA to verify the diagnosis especially for those results from RPR that are lower than 1:8. In this research, RPR results of all female patient were positive before the treatment and TPHA to confirm the results of the infection were positive for the 100% too.
Conclusions

1) Despite the fact men have higher prevalence of syphilis infection, women particularly during pregnancy remain as a challenge for the sanity. Till 2015, there was an increasing incidence of syphilis, in 2016 the cases decreased to 5.3 cases in 100 000. In Lithuania, the incidence of syphilis among women is low. The high-risk group based on age is between 20-30 and the majority of these females come from urban area.

2) In Kauno klinikos at the time of the diagnosis most of the women were in advance stages of the infection. In this research we found that most of them already are in the latent or tertiary stage with cardiovascular, neurological and ophthalmologic complications. The serological testing that was performed to make diagnosis of syphilis consisted from RPR and TPHA and both tests were found to be positive during diagnosis. Most of the women repeated RPR test one year after the treatment and it was decreased 4-fold or more.
Practical recommendations

The best way to prevent all the negative outcomes of the infection is avoiding it. The promotion of the safe sexual behaviours and the use of condoms during their sexual relations should be increased especially between the younger population who is more vulnerable and ignore the consequence of their risk practices. To inform and teach the patients to become aware about the vulnerability of the human body to sexually transmitted infections if the people do not take the necessary prevention measures and to teach them that a periodic screening can avoid a lot of complications.
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