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IMPORTANCE OF EARLY DIAGNOSIS OF LOW RESPIRATORY TRACT INFECTIONS IN PATIENTS WITH DIABETES MELLITUS

SUMMARY

The aim of the study was to assess the following parameters such as clinical and laboratory signs of inflammation syndrome, the level of diabetes regulation, localization of pulmonary infiltrates as well as bacteriological analysis of sputum specimens on acid-fast resistant bacilli and nonspecific bacterial and fungal flora in diabetic patients hospitalized with symptoms of infection and radiological infiltrates in pulmonary parenchyma confirmed during the investigation to be specific on the admission. All the examined parameters were compared with values of the patients treated for tuberculosis (TB) without associated diabetes mellitus (DM). In the study group (SG) there were 60 patients treated for TB and DM, and in the control group (CG) there were 60 of them with TB without concomitant diabetes mellitus. Average age in the SG was 59,5 years and in the CG 59 years. 40% of examinees were over 64 years of age. The average duration of symptoms in the SG was 9 and in the CG 8,9 weeks. Fever was detected in 66.7 % of the SG patients and in 61.7% of the CG patients. Leucocytosis was in ratio of 48.3/35%. Cough and expectoration were present in 71.7% of the SG and 63.3% of the CG. 90% of examinees had poor regulation of serum glucose level. There were atypical lung infiltrates on the chest X-ray in 20 % of examinees in relation to 1.7 % of the CG patients ($p<0.01$). On smear microscopy, acid alcohol resistant bacilli (ARB) were isolated in ratio of 38.3/30.0% and on Low culture ARB was isolated in ratio of 68.3/36.7%. Nonspecific bacterial and fungal flora were isolated in sputum in ratio of 68.3/36.7% ($p<0.001$). The most frequent bacterial flora in the SG was E. coli in almost 25% of those in whom nonspecific flora was isolated. Identification and differential diagnosis of specific from nonspecific etiology of pulmonary infection in diabetic patients is important because of timely treatment in immunocompromised host.

Key words: **tuberculosis, diabetes mellitus, infection**

INTRODUCTION

Many clinicians believe that diabetics have a higher tendency for developing infections (1-3). On the contrary, some earlier investigations concluded that the firm evidence for those statements did not exist (4-5). It has already been established that compensated diabetics do not get infections more than healthy people (6). But, more severe complications of glucoregulation, as well as complications on blood vessels and tissues, lead to severe form of infections which can be considered as complications in diabetic patients (7).

A few aspects of immunity have been changed in diabetic patients (5). The polymorphonuclear leukocytes function is suppressed and associated with low control of diabetes (8-10). Also, the leukocyte adherence rate is disturbed, as well as chemotaxis

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and phagocytosis (8,9). The antioxidative system involved in bactericidal activity is also compromised (11). Clinical evidence of humoral immunity is limited (5), but immune responses on standard vaccine in those patients are normal (12).

Many infections are common in diabetic patients, but some infections are typical of diabetics only. Other infections develop with higher intensity and are associated with a greater risk of complications (5).

Diabetic patients could be more predisposed to low respiratory tract infections (13). It still remains unclear whether the diabetes mellitus is an independent risk factor of higher frequency or the severity of common infections of upper and lower respiratory tract (13).

Infections caused by certain microorganisms (Staph. aureus, Gram-negative bacilli, Mycobacterium tuberculosis) develop with higher incidence, while other microorganisms (Streptococcus pneumoniae, Influenza virus) are associated with higher morbidity and mortality rate (7, 13). The latest studies suggest that mortality rate in diabetics caused by pneumonia or influenza is four times higher than in non-diabetic patients (14). The efficiency of intracellular destruction of microorganisms in diabetics could be improved with better control of the serum glucose level (9,15).

AIMS

The aim of the study was to recognize the following parameters in diabetic patients hospitalized with the symptoms of infection and radiological infiltrates in pulmonary parenchyma confirmed during the investigation to be specific:

• Clinical and laboratory signs of inflammation syndrome;

• The level of diabetes regulation and the way of the regulation before and during the hospitalization;

• Radiological localization of pulmonary infiltrates;

• Bacteriological analysis of sputum specimens on acid-fast resistant bacilli and nonspecific bacterial and fungal flora.

All the examined parameters were compared with the values of patients treated for tuberculosis (TB) without associated diabetes mellitus (DM).

MATERIALS AND METHODS

There were 60 patients treated for TB and DM in the study group (SG) and 60 of them with TB in the control group (CG). Each patient in the SG had a corresponding patient in the CG regarding sex, age and average symptoms before hospitalization.

On admission, in all the patients we assessed clinical and laboratory signs of inflammation : fever, chronic cough and expectoration - mucous or purulent, peripheral blood leukocyte count, morning serum glucose level, level of glycolic regulation on an empty stomach according to the European NIDDM Policy group criteria (well regulated - 4.4 till 6,1 mmol/l, acceptably regulated - 7.8 mmol/l, poorly regulated - > 7.8 mmol/l), chest radiography (standard postero-anterior radiography 35x43 cm, lateral radiography 30x40 cm, tomography 24x30 cm), localization of pulmonary infiltrative lesions (typical of pulmonary tuberculosis - apical and posterior segment of the upper lobe and apical segment of the lower lobe; atypical localization of pulmonary tuberculosis), cultivation of morning sputum specimen on bacterial and fungal flora and smear microscopy and parallel cultivation of the same specimen in three consecutive days by Zeihl-Neelsen and Löwenstain-Jensen.

RESULTS

There were 51.67% of men and 48.33% of women. In the CG male/female ratio was 65.0% : 35.0%. There was no statistically significant difference regarding sex in both groups (table 1).

Tabela 1. Criteria of groups' similarity

		SG	CG	Statistics
Duration of symptoms				
	Xsr ± SD	8.95±8.65 ned.	8.88±8.85 ned.	NS
Sex				
	Men	51.67%	65.0%	NS
	Women	48.33%	35.0%	
Age				
	Xsr ± SD	59.48 ± 13.53 g.	58.97 ± 13.32 g.	NS

The average age in the SG was Xsr ± SD = 59.48 ± 13.53 years, and in the CG 58.97 ± 13.32 years (no significance) (table 1). The age span of the patients was between the age of 65 and 74 in both groups, while 45% of patients in the SG were above 64 years of age (figure 1).

The average duration of symptoms before hospital admission was 8,95 weeks for patients in the SG, and 8,88 weeks for patients in the CG (n.s.)

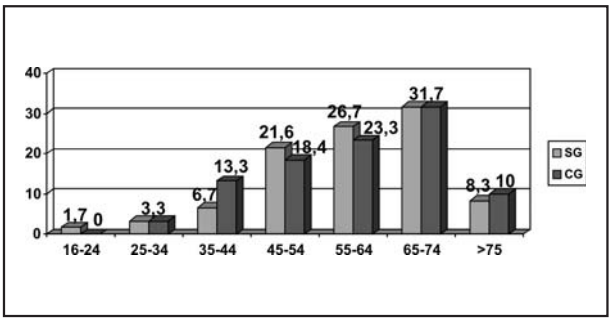

Figure 1. Age structure of examinees

Febricity was registered in 40 patients (66,7%) in the EG and 37 patients (61,7%) in the CG. Statistically significant difference was not registered (figure 2).

Leucocytosis was registered in 29 patients (48,3%) of the SG and in 21 patients (35%) of the CG with no statistically significant difference between groups.

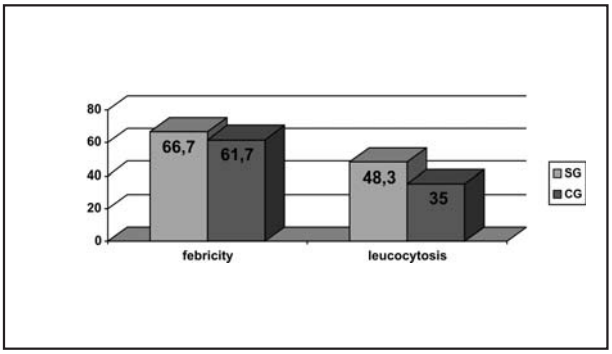

Figure 2. Febricity and leucocytosis

Chronic cough with expectoration was registered in 43 patients (71.6%) of the SG and 38 patients (63.3%) of the CG (n.s.). In the SG mucoid expectoration was present in 11 patients (18.3%) and purulent expectoration in 32 patients (53.3%) (figure 3). In the CG, the ratio was different: 21 patients (35%) had mucoid expectoration, while 17 patients (28.3%) had purulent expectoration. Statistical difference regarding the structure of expectoration is significant (p<0.01).

Well regulated values of glycemia were registered in 2 patients (3.3%) of the SG, acceptably regulated in 4 patients (6.7%) and poorly regulated in 54 patients (90%) (figure 4).

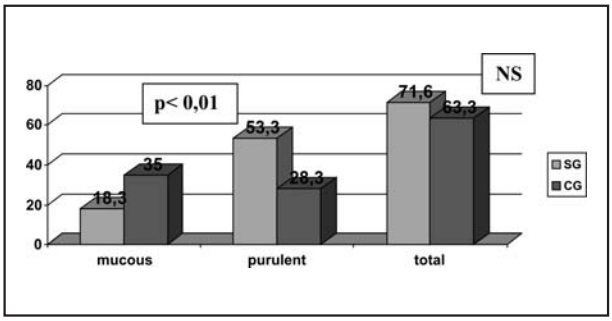

Figure 3. Cough with expectoration

Antidiabetic therapy was corrected in 51 patients (85%) of the SG. The structure of the examined group before and during the hospitalization was significant (p<0.001).

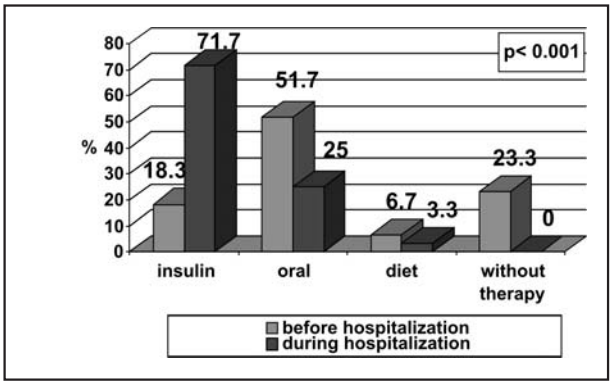

Figure 4. The way of diabetes regulation before and during hospitalization

A typical radiographic localization of pulmonary lesion was registered in 48 patients (80%) of the SG (66.7% in the upper lobe and 13.3% in the lower one) and atypical one in 12 patients (20%).

In the CG the ratio was 59 (98,3%) (81.7:16.7%) to 1 (1.7%). In the structure of relations of typical and atypical radiographic lesions the difference was significant (p<0.01). In the structure of the upper-lower lobe relations inside a typical localization, the difference was insignificant (figure 5).

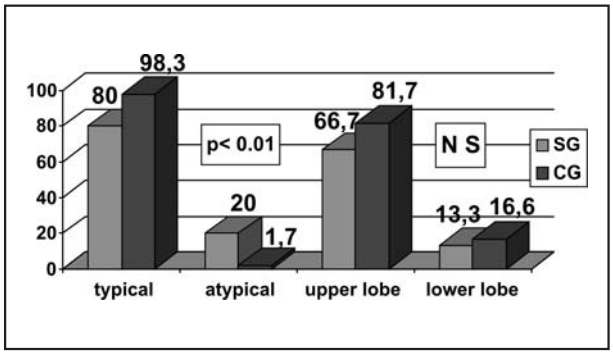

Figure 5. Typical localization of radiographic changes

By the sputum microscopy we isolated acid alcohol resistant bacilli (ARB) in 23 patients (38.3%) of the SG and 18 patients (30%) of the CG. Statistically, this difference was also insignificant.

On the Low culture ARB was isolated in 44 patients (73.3%) of the EG, and 39 patients (65%) of the CG. Statistically, this difference was insignificant (figure 6).

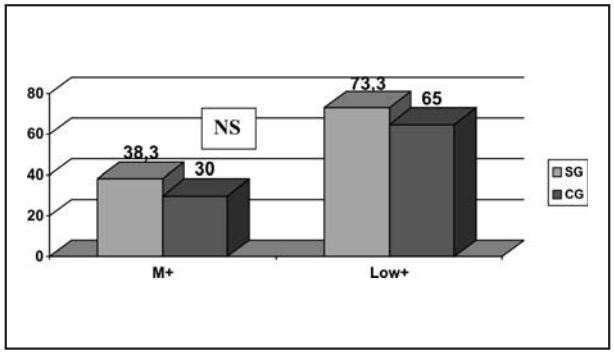

Figure 6. ARB finding in sputum

Nonspecific bacterial or fungal flora (Candida albicans) was isolated in sputum of 41 patients (68.3%) of the SG and in 22 patients (36.7%) ($p<0.001$) of the CG.

Bacteria from sputum were isolated in 33 patients (55%) of the SG and 16 patients (26.7%) of the CG. The difference was statistically insignificant. Candida albicans was isolated in 8 patients (13.3%) of the SG and 6 patients (10%) of the CG without significant difference (figure 7).

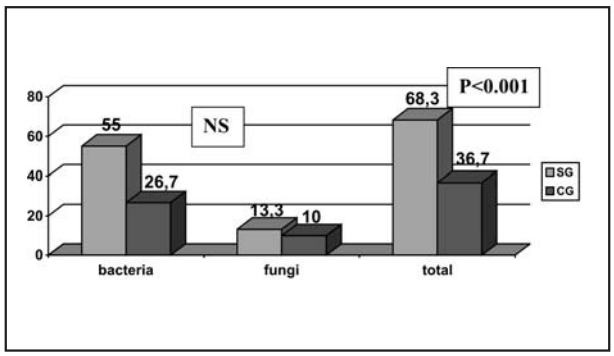

Figure 7. Nonspecific sputum flora

Nonspecific bacterial flora from the sputum was isolated in 33 patients (55%) of the SG and in 29 patients (48.3%) we registered Gram-negative and in 4 patients (6.7%) Gram-positive bacteria (figure 8).

A broader span of bacteria was isolated in the SG (overall nine) compared with patients from the CG (overall five).

In majority of the SG patients we isolated: E.coli (17%), Providentia (10%), Serratia (8.3%), Enterococcus (6.7%), Proteus mirabilis (1.7%). The same bacteria were isolated in sputum of the CG patients. Besides the aforementioned bacteria we also registered the following ones in the SG: Staphylococcus pyogenes in 6.7%, Citrobacter, Pseudomonas aeruginosa and Actinobacter 1.7% (figure 9).

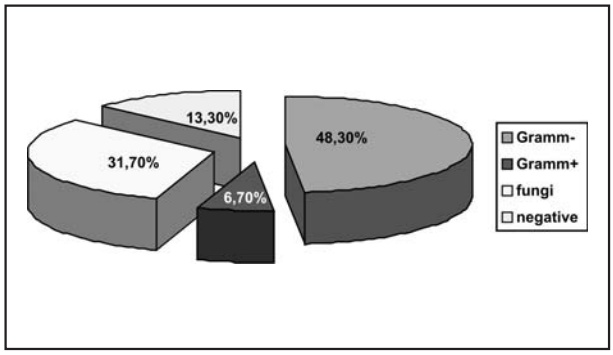

Figure 8. Distribution of Gramm- and Gramm+ bacterial flora

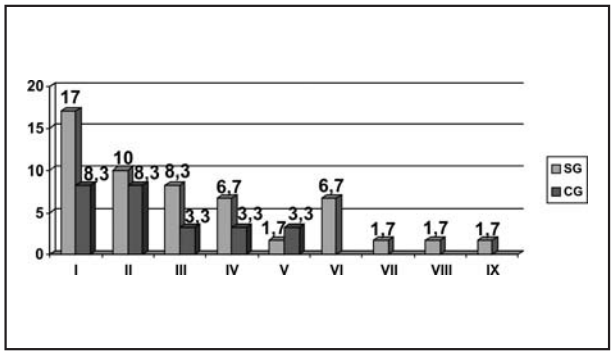

Figure 9. Isolated bacteria and their per cent distribution

I- E. coli, II- Providentia III- Seratia, IV- Enterococcus, V- Proteus mirabillis, VI-Staph. pyogenes, VII-Citrobacter, VIII-Pseud. aeruginosa, IX-Acinetobacter

DISCUSSION

The most frequent bacterial infections in diabetics patients are pulmonary tuberculosis, urinary tract infections and pneumonia (3).

Pathological changes on the chest radiography could be the consequence of tuberculosis destroyed lung as well as many other diseases. Therefore, radiography is not specific of tuberculosis (16). In order to ascertain tuberculosis infiltrate origin, further investigations are needed, and irrefutable proof can be obtained only by bacteriology (17).

By sputum smear, diagnoses were confirmed in one third of the patients, by culture, for which the results can be obtained after 6-8 weeks, diagnoses were confirmed in the other third, and the last third of the patients remains bacteriologically unconfirmed. Fast methods of identification, such as radiometric method (BACTEC) and PCR amplification of DNA (PCR - polymerase chain reaction) are expensive and in ordinary clinical practice unavailable for the routine use. On the other hand, etiologi-

cal cause of pneumonia remains unconfirmed in more than 50% of cases, even in cases with more detailed investigations (18).

Tuberculosis is more frequent in diabetic patients (19). This fact is important in the current epidemiological situation, when about 8 to 10 million people get the disease annually and when the estimation is that by 2005 about 300 million people will have suffered from DM (19), since the trend is constantly rising. That is why we should perform medical and radiographic examinations in all diabetic patients twice a year (19).

The older population, due to a decreased immunity and frequent concomitant diseases, is at risk of pulmonary infections, especially of tuberculosis (20). This is confirmed by the age of the SG patients, where 40% of them are above 65 years of age.

In diabetics with tuberculosis, the most dominant symptoms were temperature, swelling and cough (21). In the diseased with poor regulation of diabetes, leucocytosis is more present than in the patients with more favorable course of the disease (22). In our investigation, febricity and leucocytosis are increased in the SG patients.

Tuberculosis incidence among diabetics increases with diabetes duration and with increasing of insulin dose needed for its regulation. At the same time, tuberculosis leads to worsening of diabetes, which demands a greater insulin dose (19). In the SG patients the correction of antidiabetic therapy needed to be carried out in 85%, The values of glycemia conditioned the introduction of insulin therapy in 71,1% of patients compared to 18,3% of patients before the onset of tuberculosis.

Atypical radiological presentation of pulmonary lesions (23) is seen in diabetic patients, which confirms our investigation.

Nonspecific bacterial and fungal flora is found in sputum of 68,3% of patients. For clinician, those findings are important in the sense of differential diagnosis of pulmonary infection and earlier adequate treatment.

CONCLUSION

To conclude, diabetics with tuberculosis have more frequent manifestations of clinical signs of inflammatory syndrome compared to non-diabetic tuberculosis patients.

Diabetes regulation during the infection is extremely poor.

Percentage of ARB finding in sputum is higher in diabetic patients, while the findings' values of nonspecific bacterial and fungal flora are even more increased.

Nonspecific bacterial and fungal flora in sputum of tuberculosis diabetics, besides the frequent dominant symptoms of this disease and atypical radiological presentation, can condition the failure of tuberculosis recognition and untimely treatment. The consequences could be serious: advancing form of tuberculosis, increasing percentage of the diseased coughing out bacilli into the environment, increasing thus the mortality rate.

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ZNAČAJ RANE ETIOLOŠKE DIJAGNOZE PLUĆNE INFEKCIJE KOD DIJABETIČARA

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SAŽETAK

Cilj rada bio je da kod dijabetičara hospitalizovanih sa znacima infekcije donjeg respiratornog trakta i radiografskim promenama na plućima, a za koje je tokom dijagnostičkog postupka dokazano da su specifične, na početku hospitalizacije sagledamo kliničke i laboratorijske znake zapaljenskog sindroma, stepen regulisanosti dijabetesa, lokalizaciju plućnih promena i bakteriološku analizu sputuma na bakterije, gljive i acido-rezistentan bacil (ARB). Sagledane parametre smo uporedili sa nalazom kod pacijenata lečenih od tuberkuloze (TB) bez pridruženog dijabetesa (DM). U ispitivanoj grupi (IG) bilo je 60 dijabetičara lečenih od tuberkuloze, a u kontrolnoj (KG) 60 pacijenata sa tuberkulozom bez pridruženog dijabetesa. Prosečna starost u IG grupi bila je 59.5, a u KG 59 godina. 40% ispitanika bilo je starije od 64 godine. Prosečno trajanje simptoma u IG je bilo 9, u KG 8.9 nedelja. Kod 66.7% pacijenata IG i 61.7% KG grupe bila je prisutna febrilnost. Leukocitoza je bila u odnosu 48.3 : 35%. Kašalj sa iskašljavanjem bio je prisutan kod 71.7% u IG i 63.3% u KG grupi. Loše regulisane vrednosti glikemije imalo je 90% ispitanika. Kod 20% ispitanika lokalizacija plućnih infiltrata je bila atipična, u odnosu na l.7% u KG (p<0.01). Mikroskopijom razmaza sputuma ARB je izolovan u odnosu 38.3 : 30.0%, a Low kulturom 73.3 : 65%. Nespecifična bakterijska i gljivična flora je izolovana iz sputuma u odnosu 68.3 : 36.7% (p<0,001). Najzastupljenija bakterija u IG grupi bila je E. coli kod skoro 25% onih kod kojih je izolovana nespecifična flora. Identifikacija uzročnika i diferencijalna dijagnoza specifične od nespecifične etiologije plućne infekcije kod dijabetičara značajna je zbog što ranijeg započinjanja adekvatnog tretmana u imunokompromitovanom organizmu.

***Ključne reči*: tuberkuloza, diabetes mellitus, infekcija**