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Microbial pathogens in moderate to severe diabetic foot infections

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Foot infections are the most common complications in diabetic patients and common cause of morbidity and mortality. They require prompt diagnosis and involvement of a multidisciplinary team in their treatment. Prospective study to define the etiology of the deep diabetic foot infections and its specific characteristics concerning the adequate empiric antimicrobial therapy was done. The study included 50 patients, who underwent minor amputations due to moderate to severe infection of the foot. All specimens for microbiology testing were taken by biopsy or aspiration during surgery. Specimens cultivation, identification of the isolated microorganisms and their susceptibility towards antimicrobial agents were performed by conventional methods and automated systems. Diabetic foot infections were predominantly polymicrobial; 42 (84%) of the cases, caused by associations between two, three and four different pathogens. Mixed infections caused by aerobic and anaerobic bacteria were found in 17 patients (34%). Gram-positive bacteria were the prominent microbial pathogens in both monobacterial and polymicrobial infection; mostly *Streptococcus agalactiae and Staphylococcus aureus*. Gram-negative aerobic bacteria presented 33.3% of all isolated bacteria, predominantly members of Enterobacteriaceae family. Obligate anaerobes represents 16.66% of all isolated bacteria and were causative organisms in 17 (34%) of the patients, more than the other *Bacteroides fragilis* group and anaerobic streptococci. The strains isolated were susceptible to the recommended antibacterial agents for treatment of moderate and severe diabetic foot infections (DFIs). The optimal approach to DFIs requires immediate surgical intervention, revascularization in the setting of a multisegment vascular lesions, microbiological examination of suitable clinical materials and appropriate antibacterial therapy for empiric treatment of aerobic and anaerobic pathogens

Key words: Diabetic foot, infection, microbial pathogens.

INTRODUCTION

Diabetes mellitus is a chronic disease that poses a serious public health problem worldwide. Different researchers estimated that in 2011, between 350 million (6.6% of the population) (Lepantalo et al., 2011) to 366 million people worldwide were living with diabetes (IDF Diabetes Atlas, 2011). It is predicted that by 2030 the

numbers will raise to 552 million with half of them living in Asia (IDF Diabetes Atlas, 2011). Although it is reported that in rural and urban regions in west and east Asia the rate of the disease is less than 3%, the rate in urban and suburban population in South Africa is 3 - 10% which makes it comparable with rates in developed countries (Mbanya et al., 2010). In Europe more than 55 million suffer from diabetes mellitus and estimates for 2025 cite a total over 65 million patients (Lepantalo et al., 2011). Foot infections are the most common complication in diabetic patients and a common cause of morbidity and mortality. At least half of all non-traumatic lower limb amputations are performed on diabetic patients (Nolan and Chapman, 2003), as in 5 - 8% of cases require major amputation within one year (Lepantalo et al., 2011). Therefore diabetic foot infections (DFIs) require prompt diagnosis and involvement of a multidisciplinary team in their treatment. Early surgical treatment, combined with identification of the etiology of the infection and adequate intravenous antimicrobial therapy significantly reduces the risk of major (above ankle) amputation in these patients (Tan, 2006).The aim of this prospective study was to define the etiology of the deep DFIs and its specific characteristics concerning the adequate empiric antimicrobial therapy.

MATERIALS AND METHODS

Study population

This prospective study includes 50 patients with diabetes type 1 and 2 who have been treated at Departments of Vascular surgery (24 patients) and Septic surgery (26 patients) at University Hospital of Pleven and suffered minor amputation due to moderate or severe infection of the foot between February 2012 and February 2014. In 13 of the patients foot ulcers were neuropathic and the remaining 37 – ischemic or combined.

All 50 specimens for microbiological examination were obtained by tissue or bone biopsy, or aspiration during surgery and were immediately transported to the laboratory. The study did not include materials taken with swab techniques from surface of the ulcers and debrided necrotic materials.

Methods

The evaluation for presence of ischemia was done by a vascular surgeon. Patients with manifested limb ischemia were treated in Department of Vascular Surgery. The methods used for verification and determination of the extend of the ischemia include palapation of dorsalis pedis and tibialis posterior arteries, ankle-brachial index (ABPI<0,9); ultrasonography and CT-angiography. The presence of neuropathy was determined by electromyography.

The specimens were inoculated onto anaerobic media – Shaedler agar (BBL, Becton-Dickinson and Co., Sparks, MD, USA) supplemented with 5% sheep blood and thioglycollate broth (BBL,Becton-Dickinson and Co., Sparks,MD,USA) and incubated at anaerobic conditions at 37°C for 2-4 days. If the presence of anaerobic bacteria was suspected, this was confirmed by aero-tolerance testing. Final identification of all anaerobic isolates was performed by Gram-stain and RapidAPI ID32A (miniAPI, bioMerieux, France). The susceptibility of anaerobic bacteria towards antimicrobial agents was not performed.

Aerobic cultures were performed on blood agar (5% sheep blood), Levine agar and trypticase soy broth (BBL, Becton-Dickinson and Co., Sparks, MD, USA) and incubated at 35°C for 24 h in ambient air. Identification of the aerobic and facultative anaerobic bacteria isolates was performed by rapid tests and conventional methods (Forbes et al., 2002), followed by identification with automated system Vitek 2 (bioMerieux, France) with GN REF21341\GP REF21342. The susceptibility to antimicrobial agents of aerobic and facultative anaerobic bacteria was performed by disk-diffusion method on Muller-Hinton II agar (BBL, Becton-Dickinson and Co., Sparks,MD,USA), supplemented with 5% sheep blood only for alpha and beta-haemolythic streptococci. The results were confirmed via automated system Vitek 2 (card AST-N204 REF412865/AST N222 REF413083/AST-GP REF22226).

RESULTS

Of the 50 patients included in the study, 30 were male and 20 were female.The average age of patients was 61.4 years (ranged from 31 to 86 years). All patients had poorly controlled diabetes - average blood glucose levels on admission (21.29 mmol/l) (from 4.4 to 47 mmol/l) and moderate levels of glycated hemoglobin (9.57%) (from 6.95% to 10.73%). All patients had a limb-threatening infections diagnosed clinically based on the local and systemic signs of inflammation, according to the following criteria: cellulitis > 2 cm, edema, pain, lymphangitis, purulent discharge and bad odor, fever, hypotension, ischemic changes and poor general condition (Frikberget al., 2003; Lepantalo et al., 2011). Twenty-two patients were in the third stage (deep ulcer with osteitis), 18 - in fourth (partial foot gangrene) and 10 - in the fifth stage (whole foot gangrene) of infection according to the Wagner' s classification, which is comparable with Texas University Diabetic Foot Scale (Wagner, 1987; Oyibo et al., 2001). In 13 of the patients, foot ulcers were neuropathic and the remaining 37 - ischaemic or combined (neuro-ischemic). Twenty four of the patients were with severe ischemia (ABPI<0,9) and other 13 - with mild ischemia.

All cultured specimens were positive for bacterial growth. A total of 120 bacterial strains were isolated. The range of all organisms was 1 to 4 per specimen resulting in an average of 2.4 organisms per specimen. The types and number of bacterial isolates are presented in Table 1.

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Table 1. The types and number of bacterial isolates.

Microorganism	Number of strains and percentage
Gram-positive aerobes	**60 (50,00%)**
Staphylococcus aureus	22
Staphylococcus epidermidis	7
Streptococcus agalactiae	15
Streptococcus pyogenes	1
Streptococcus viridans	1
Enterococcus faecalis	10
Enterococcus faecium	1
Corynebacterium xerosis	3
Gram-negative aerobes	**40 (33,33%)**
Escherichia coli	13
Klebsiella pneumoniae	3
Klebsiella oxytoca	3
Klebsiella ornithinolytica	1
Enterobacter cloacae	3
Serratia marcescens	2
Proteus mirabilis	6
Providencia rettgeri	1
Morganella morganii	2
Citrobacter freundii	1
Citrobacter diversus	1
Pseudomonas aeruginosa	3
Acinetobacter baumannii	1
Anaerobes	**20 (16,66%)**
Bacteroides fragilis	5
Bacteroides ovatus	1
Bacteroides fetaiotaomicron	1
Peptostreptococcu sanaerobius	6
Propionibacterium acnes	2
Veillonella parvula	2
Prevotella intermedia	1
Bifidobacterium spp.	1
Anaerococcu sprevottii	1
Total	**120**

Only in eight patients (16% of the cases) was limb-threatening DFI monobacterial. In six of them causative agents were Gram-positive bacteria: *S.aureus* (3) and *S.agalactiae* (3), and Gram-negative bacteria (*P. aeruginosa* or *E.coli*) in another two. In 42 patients (84%), the infections were polymicrobial, caused by: two types of organisms (19), three (19) and four types of organisms (4). Mixed infections, caused by aerobic and anaerobic bacteria were found in 17 patients (34%). There is great variety in the nature of microbial associations (Figure 1, Tables 2 and 3). Associations between Gram-positive and Gram-negative bacteria were dominant (12, 28.57%), followed by the associations between two or more species of Gram-positive bacteria (9, 21.42%), and rarely other associations. Gram-positive aerobic bacteria are involved in 33 (78.57%) of the cases of polymicrobial infections, and Gram-negative aerobic bacteria in (26, 61.90%) cases.

Obligate anaerobes represent 16.66% of all isolated bacteria and were causative pathogens in 17 (34%) of the cases. Anaerobes were never isolated in the cases of monobacterial infection, but always in associa-tion with other anaerobic or aerobic bacteria.

Gram-positive aerobic bacteria are leading microbial pathogens in both monobacterial andpolymicrobial infec-tions. They comprised 60% of the aerobic organisms and 50% of all strains isolated. *Staphylococcus* species were the most common organisms detected, followed by beta-hemolytic streptococci and enterococci. The predominant aerobic species was *S. aureus* isolated in three cases of monobacterial and in other 19 cases of polymicrobial infections.

The isolated strains showed 72.7% resistance to Penicillin G and 18.18% resistance to Erythromycin and Clindamycin. All isolated strains were susceptible to Methicillin, Ciprofloxacin, Vancomycin and Tigecycline. All strains of *S. epidermidis* were isolated in association with other highly pathogenic bacteria. Three of the strains were methicillin-resistant and showed resistance to other groups of antimicrobials. Streptococci were the second most frequently isolated Gram-positive pathogens, as the dominant role of *S.agalactiae* is unquestionable. All strains of *S. agalactiae* were susceptible to Penicillin G, ciprofloxacin, levofloxacin, and chloramphenicol, while three were resistant to Erythromycin and Clindamycin. Enterococci were isolated from 11 patients, always in association with other bacteria. Four of the isolated strains were resistant to ciprofloxacin, two to Ampicillin and two to Gentamicin. All strains isolated were susceptible to glycopeptides and Tigecycline (Table 4).

Gram-negative aerobic bacteria comprised 40% of aerobes and 33.3% of the all isolated bacteria. Members of the family *Enterobacteriaceae* were predominant. *E. coli* and *Klebsiella-Enterobacter-Serratia* group were the most often isolated pathogens. 100% of isolated strains were susceptible to Imipenem, Meropenem, Piperacillin/Tazobactam, Cefoperazone/Sulbactam, Amikacin, Tobramycin and Tigecycline. Three of the strains were extended spectrum beta-lactamases producers.

Of the all isolated Gram-negative organisms, 75% were resistant to Ampicillin, 42.5% to amoxicillin/clavulanic acid, 20% to piperacillin, 5% to piperacillin/tazobactam, 55% to cephalothin, 37.5% to cefuroxime, 12.5% to cefoxitin, 7.5% to ceftazidime and cefepime, 10% to gentamicin, 7.5% to amikacin, 10% to tobramycin, 7.5% to ciprofloxacin and levofloxacin, 7.5% to tigecycline, and 37.5% to trimethoprim/sulfamethoxazol (Table 5).

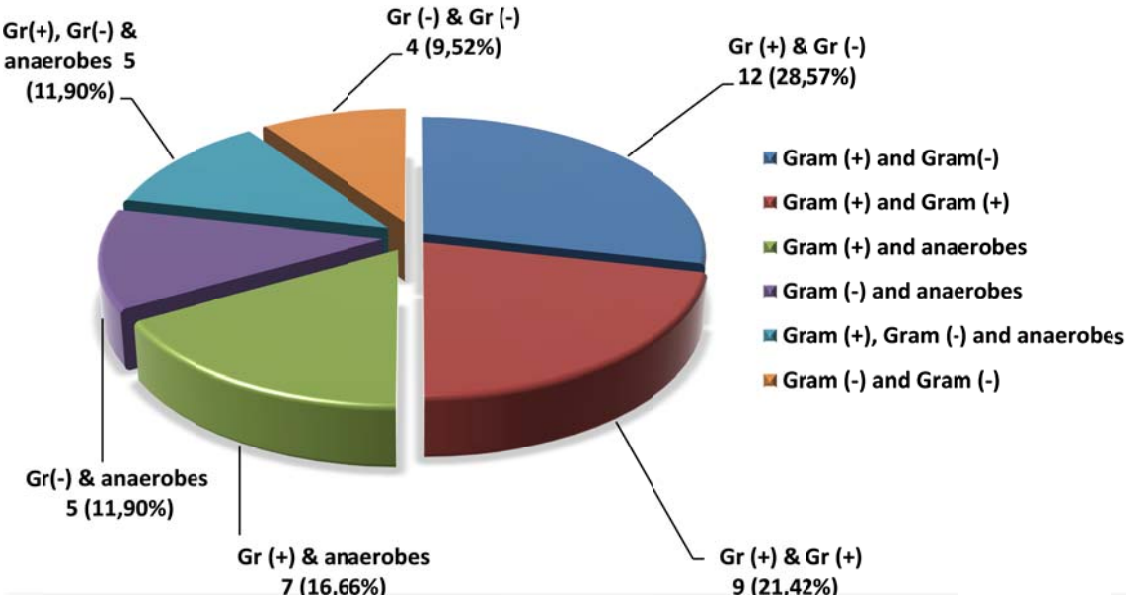

Figure 1. Share of different microbial associations in polymicrobial diabetic foot infection

Table 2. Microorganisms isolated from patients, treated in Department of Vascular Surgery.

Gender	Microorganism
F	*S. aureus + P. mirabilis + P. rettgeri + V. parvotela*
F	*S. aureus*
M	*P. mirabilis + P. anaerobius*
F	*S. agalactiae*
M	*S. agalactiae + S. epidermidis*
M	*S. agalactiae*
M	*S. agalactiae + S. aureus + S. marscescens*
M	*S. agalactiae + S. aureus*
F	*K. pneuminiae + E. cloacae*
M	*S. aureus* + E. *coli* + K. *oxytoca* + C. *xerosis*
M	*S. aureus* + A. *baumanii*
F	*S. epidermidis* (MRSE) + *C. xerosis* + *P. anaerobius*
M	*E. coli + E. faecalis*
M	*S. aureus*
M	*C. freundii + E. faecalis + B. tetaiotaomicron*
M	*E. coli + E. faecalis + P. anaerobius*
M	*P. aeruginosa + S. marcescens + S. aureus*
M	*S. agalactiae + S. aureus*
M	*S. agalactiae + S. aureus*
M	*P. mirabilis + K. oxytoca + E. coli*
M	*S. aureus*
M	*M. morganii + E. coli + S. agalactiae*
F	*S. aureus + S. pyogenes*
M	*E. faecalis + A. prevottii*

Table 3. Microorganisms isolated from patients, treated in Department of Septic Surgery.

Gender	Microorganism
M	*P. aeruginosa*
M	*B. fragilis + E. faecalis + S. epidermidis*
F	*E. coli + P. anaerobius + V. parvula*
M	*E. cloacae + S. epidermidis + B. fragilis*
F	*S. viridans + S. epidermidis + B. fragilis*
M	*S. aureus + P. mirabilis + E. faecalis*
F	*E. coli + S. epidermidis + C. xerosis*
F	*E. coli + E. faecalis + S. epidermidis (MRSE)*
F	*S. agalactiae + S. aureus + P. anaerobius*
F	E. *coli*
F	*E. faecalis + B. ovatus*
M	*E. coli + K. ornitinolytica + B. fragilis*
F	*S. aureus + B. fragilis*
F	*E. coli + M. morgagnii + K. oxytoca*
M	*S. aureus + E. faecalis*
F	*S. aureus + E. faecium + E. coli + B. fragilis*
M	*S. aureus + E. cloacae*
F	*S. agalactiae + S. aureus + K. pneumoniae*
M	*P. mirabilis + P. acnes*
F	*P. aeruginosa + P. anaerobius + P. acnes*
F	*E. coli + E. faecalis + C. diversus + S. agalactiae*
M	*S. agalactiae + S. aureus*
F	*S. agalactiae + S. aureus*
M	*P. mirabilis + K. pneumoniae* (ESBLs)
M	*S. agalactiae + S. aureus*
M	*S. agalactiae*

Table 4. Resistance to antimicrobial agents of Gram-negative aerobic and facultative anaerobic bacteria (NT-not tested).

Antimicrobial agent	Fam. Enterobacteriaceae				Non-fermenting glucose bacteria	Total resistance (%)
	E. *coli* (13 strains)	KES Group (12 strains)	PPM Group (9 strains)	Citrobacter spp. (2 strains)		
Ampicillin	9	11	4	2	4	30 (75%)
Amoxicillin/Clav. Acid	4	6	2	1	4	17 (42,5%)
Piperacillin	4	3	0	0	1	8 (20%)
Piperacillin/Tazobactam	0	0	0	0	2	2 (5,0%)
Cephalotin	9	8	3	2	NT	22 (55.0%)
Cefuroxime	6	6	2	1	NT	15 (37,5%)
Cefoxitin	2	1	1	1	NT	5 (12,5%)
Cefotaxime	1	2	0	0	NT	3 (7,5%)
Ceftriaxone	1	2	0	0	0	3 (7,5%)
Ceftazidime	1	2	0	0	0	3 (7,5%)
Cefapime	1	2	0	0	0	3 (7,5%)
Cefoperazone/Sulbactam	0	0	0	0	0	0%
Imepenem	0	0	0	0	0	0%
Meropenem	0	0	0	0	0	0%
Gentamicin	1	1	0	0	2	4 (10,0%)
Amikacin	0	0	0	0	3	3 (7,5%)
Tobramicin	0	0	0	0	4	4 (10,0%)
Ciprofloxacin	0	2	0	0	1	3 (7,5%)
Levofloxacin	0	2	0	0	1	3 (7,5%)
TMP/SMZ	7	2	4	0	2	15 (37,5%)
Tigecycline	0	0	0	0	3	3 (7,5%)

Table 5. Resistance to antimicrobial agents of Gram-positive aerobic and facultative anaerobic bacteria.

Antimicrobial agents	*Staphylococcus aureus*	Coagulase-negative staphylococci	Streptococcus B-haemolyticus	Enterococcus spp.
	(22 strains)	(7 strains)	(16 strains)	(11 strains)
Penicillin	16 (72, 7%)	7 (100%)	0	NT
Methicillin/Oxacillin	0	3 (42, 8%)	NT	NT
Erythromycin	4 (18, 18%)	4 (57, 14%)	3 (18, 75%)	NT
Clindamycin	4 (18, 18%)	4 (57, 14%)	3 (18, 75%)	NT
Ciprofloxacin	0	2 (28, 57%)	0	4 (36, 36%)
Levofloxacin	NT	NT	0	0
TMP/SMZ	0	2 (28,57%)	NT	NT
Vancomycin	0	0	NT	0
Teicoplanin	0	0	NT	0
Linezolid	0	0	NT	0
Chloramphenicol	NT	NT	0	NT
Ampicillin	NT	NT	NT	2 (18, 18%)
Gentamycin 120	0	0	0	1 (9, 09%)
Tigecycline	0	0	0	0

The follow-up period ranges from one month to two years. In two of the patients a major amputation was performed during the follow-up period despite the vascular reconstruction and the adequate antibacterial therapy. In both patients the infection involved planta pedis and os calcanei and was polymicrobial, caused by

association of three types of bacteria: in the first one *S. aureus*, *P. aeruginosa* and *S. marcescens* and in the other S. *agalactiae*, *E. coli* and *M. morganii*.

DISCUSSION

During the last 30 years many studies on etiology of diabetic foot infection have been conducted. The results of these studies are very different because of the different specimen collection techniques and also different laboratory techniques which sometimes were not suitable for growing of anaerobic and other fastidious micro-organisms. The variable results can also be explained by the severity of the infection, previous hospitalizations, different number of examined patients and antibacterial treatment in the past. Our study only included patients with moderate to severe infections of the foot which suffered mild amputation and did not receive antibacterial therapy for more than 24 h in the previous three days. Despite the different results from the studies all, authors agree that the limb-threatening infections are mostly polymicrobial (Nolan and Chapman, 2003; Citron et al., 2007; El-Tahawy, 2000; Lipsky et al., 2012). In huge multicenter study which included 433 patients with diabetes, Citron et al. (2007) reported that only 16.2% of 427 positive samples were monobacterial while the rest were polymicrobial. Other authors reported different relative share of polymicrobial infections, which widely varies: from 35% (Bansal et al., 2008); 64.4% (Anandi et al., 2004); 75% (Al Benwan et al., 2012) to 80% (Alsaimary, 2009). The number of the isolated microorganisms per specimen also varies: 3 - 5 (Bansal et al., 2008; El-Tahawy, 2000) to 1 - 13 according to Citron et al. (2007), with average of 1.5 to 3.8 microbial species per positive sample, respectively. There is also a difference in the most common causative agent in different parts of the world. In Asia and Africa most significant are the Gram-negative aerobic rods (Anandi et al.,2004; Alsaimary, 2009; El-Tahawy, 2000; Al Benwan et al.,2012), while in Europe and North America Gram-positive aerobic bacteria are predominant (Lipsky et al., 2004; Blanes Mompo, 2011).

The gold standard for examination of DFIs is deep materials from lesions, taken during surgical interventions and also bone biopsies (Lipsky et al., 2004; Louie et al., 1976). Superficial samples taken with sterile swab are known to be uncertain because of the presence of normal skin flora, which role for the development of infection is next to impossible to assess (Armstrong and Lavery, 1998; Citron et al., 2007; Lipsky et al., 2004).

Literature data shows that the most commonly isolated microorganisms from foot infections in diabetic patients are Gram-positive aerobic bacteria (Frykberg, 2003). According to the study their share varies from 28% (El-Tahawy, 2000) to 63% (Citron et al., 2007) and according to Lipsky et al. (2004) they can even reach 89% in mild infections and in patients who did not admit antibiotics. In these patients *S. aureus* and coagulase-negative staphylococci have leading role (Bader, 2008; El-Tahawy, 2000; Nolan and Chapman, 2003). In molecular studies *S. aureus* was the most commonly isolated micro-organism (Dowd et al., 2008). In our study, staphylococci were isolated from 29 patients (58%) and again *S. aureus* is most common pathogen with share of 44% (22 cases). In seven other patients coagulase-negative staphylococci (*CNS*) were isolated in deep tissues which leads to the conclusion that they were involved in the development of the infection. Three of the isolated *CNS* strains were methicilin-resistant (10.34%). This confirms the thesis of other authors that the share of *MRSA* and *MRCNS* is relatively low and that these multiresistant bacteria are more usual in patients with multiple hospitalizations (Abdulrazak et al., 2005). According to the same authors *S. aureus* and beta-hemolytic streptococci are dominant in patients with moderate and severe infection of the foot which were previously untreated. Other authors state that *S. aureus* (including *MRSA*), *S. agalactiae* and *S. pyogenes* are predominantly isolated from superficial ulcers smaller than 2 cm while ulcers bigger than 2 cm and involving deep tissues are more often polymicrobial. In cases with extensive local inflammation plus systemic toxicity it is usual for the infection to be polymicrobial (Gilbert et al., 2008).

We isolated streptococci from 17 patients, 16 of which had beta-hemolytic and in only one patient had *Streptococcus viridans*. The most common species Isolated was *S. agalactiae* - 15 patients (30.0%). *S. agalactiae* indeed is the second most common pathogen in DFIs (Citron et al., 2007; Nolan and Chapman, 2003). *S. agalactiae* has bigger affinity towards glucose related to other species from this genus and also ability to use both simple and complex carbohydrates for its metabolism (Yanai et al., 2012). Risk factors for such infections include diabetes, male gender, age above 60 years, chronic liver and kidney disease, oncologic diseases and AIDS (Murray et al., 2013; Yanai et al., 2012). *S. agalactiae* is a well-known pathogen in neonatal meningitis and infections in pregnant women. In the last two decades the aggressive antibacterial prophylaxis reduced the incidence in these groups (Murray et al., 2013).

According to Skoff et al. (2009) 56% from patients with *S.agalactiae* infections of skin, bones and soft tissues were with diabetes. In our study 10 of the patients with *S. agalactiae* DFIs were male and 5 female. Average age of the patients was 60.2 years. Most of the patients were significantly older than 60 years. In three of our cases *S.agalactiae* was isolated in pure culture, while in other 10 in association with *S. aureus*. For the analyzed period in our laboratory, we isolated 42 strains *S. agalactiae* from patients treated in different clinics of University

Hospital. Eight of them were isolated from children and newborn and the rest of them - from adult patients. Twenty two strains (52.38%) were isolated from diabetic patients, which is 64.70% of the all isolated from adult strains.

We isolated *Enterococcus* species from 11 (22%) patients, always in association with other bacteria with more expressed pathogenic potential. The share of these bacteria varies in different studies - from 14.9% (Ozer et al., 2012) to 35.7% (Citron et al., 2007). We support the thesis of Nolan and Chapman (2003) that the role of enterococci as well as the role of *Corynebacterium* spp. is hard to be evaluated especially in the cases of microbial associations. Other authors also accept that the role of *Enterococcus spp*. in DFIs is unclear (Gilbert et al., 2008). Enterococci can be part of the normal skin flora and not to be relevant with the infectious process excluding the cases when they were isolated in pure culture or the patient is not responding to therapy which is not targeted against them (Nolan and Chapman, 2003).

Gram-negative bacteria from *Enterobacteriaceae* family are common for DFIs with incidence of 24-27% (Nolan and Chapman, 2003) and even up to 40% according to some authors (El-Tahawy, 2000). In India the percentage of these isolates is equal even higher than the strains of *S.aureus* (Singh et al., 2009; Umadevi et al., 2011). In our study the predominant species from this group was *E.coli* unlike other studies which point *P. mirabilis* as leading causative agent from this family. (Anandi et al., 2004; El-Tahawy, 2000). The members *Enterobacteriaceae* family are usually associated with other pathogens in polymicrobial DFIs (Blanes Mompo, 2011; Citron et al., 2007).

Currently there are multiple antibacterial regiments for treatment of diabetic foot infections according to the severity of the infection (Nolan and Chapman, 2003; Lipsky et al., 2004; Gilbert et al., 2008). The strains we isolated were susceptible towards recommended antibacterial agents for treatment of moderate and severe DFIs. We observe low incidence of *MRSA*. The aerobic isolates showed good susceptibility towards Ciprofloxacin and Levofloxacin unlike some studies that reported 29% resistant towards Ciprofloxacin (BlanesMompo, 2011). These results allow us to prefer intravenous application of fluoroquinolones as monotherapy or in combination with Clindamycin according to the efficiency: cost index. In cases of suspicion for anaerobic infection we add Metronidazole to the empiric therapy.

Conclusion

The optimal approach to DFIs requires immediate surgical intervention, microbiological examination of suitable clinical materials and appropriate antibacterial therapy for empiric treatment of aerobic and anaerobic pathogens. Due to the variations in the spectrum of the leading microbial species causing diabetic foot infections in different parts of the world, in different parts of one country and even in different hospitals, the antibacterial therapy must be complied with the typical causative agents of DFIs in the current region.

Conflict of Interest

The author(s) have not declared any conflict of interests.

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