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Surveillance of antibiotic susceptibility in a Swedish Burn Center 1994–2012

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ABSTRACT

Patients with burn trauma are at risk for infections caused by antibiotic resistant bacteria (ABR) with subsequent increase in morbidity and mortality. As part of the Swedish strategic program against antibiotic resistance in intensive care (ICU-Strama), we have surveyed the distribution of species and ABR in isolates from patients admitted to a Swedish burn center at Linköping University Hospital from 1994 through 2012. In an international comparison Strama has been successful in reducing the antibiotic consumption among animals and humans in primary care. The aim of this study was to investigate the antibiotic consumption pressure and resistance rates in a Swedish burn unit.

Methods: Microbiology data, total body surface area (TBSA), patient days, and mortality were collected from a hospital database for all patients admitted to the Burn Center at the University Hospital of Linköping from April 1994 through December 2012.

Results: A total of 1570 patients were admitted with a mean annual admission rate of 83 patients (range: 57–152). 15,006 microbiology cultures (approximately 10 per patient) were collected during the study period and of these 4531 were positive (approximately 3 per patient). The annual mean total body surface area (TBSA) was 13.4% (range 9.5–18.5) with an annual mortality rate of 5.4% (range 1–8%). The MRSA incidence was 1.7% (15/866) which corresponds to an MRSA incidence of 0.34/1000 admission days (TAD). Corresponding figures were for *Escherichia coli* resistant to 3rd generation cephalosporins (ESBL phenotype) 8% (13/170) and 0.3/TAD, *Klebsiella* spp. ESBL phenotype 5% (6/134) and 0.14/TAD, carbapenem

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Abbreviations: R, Resistant; I, Intermediary Resistant; S, Susceptible; ABR, Antibiotic Resistant Bacteria; C CVC, Central Venous Catheter; CNS, Coagulase-negative staphylococci; DDD, Defined Daily Dose; ESBL, Extended Spectrum Beta-lactamase; EUCAST, European Committee on Antimicrobial Susceptibility Testing; (B)ICU, (Burn) Intensive Care Unit; ICU-STRAMA, (Intensive Care Unit) Swedish strategic program against antibiotic resistance; LOS, Length of Stay; MRSA, Methicillin resistant *Staphylococcus aureus*; Pip-Taz, Piperacillin-Tazobactam; Sp(p), Species; STRAMA, Swedish Strategic Program Against Antibiotic Resistance; TAD, Thousand Admission Days; TBSA, Total Body Surface Area; TMX, Trimethoprim/Sulfamethoxazole; VRE, Vancomycin resistant *Enterococcus*.

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resistant *Pseudomonas aeruginosa* 26% (56/209) and 1.28/TAD, and carbapenem resistant *Acinetobacter* spp. 3% (2/64) and 0.04/TAD.

Conclusions: Our results show a sustained low risk for MRSA and high, although not increasing, risk for carbapenem resistant *P. aeruginosa*.

1. Introduction

Infections are still a major problem in severe burns receiving intensive care [1–9]. The overall morbidity and mortality of burn patients has decreased over the years, much due to improvements in early surgical intervention, wound care, and intensive care treatment [10–15].

Since approximately 75% of burn mortality is related to infections [1–3,16–19], epidemiologic surveillance of these, including antibiotic resistance, is important to guide empiric treatment. Unwarranted usage of broad-spectrum antimicrobial agents leads to increased selection of resistant microbes. This is seen globally [20–31] with increasing numbers of reports on antibiotic resistant bacteria (ABR) such as methicillin resistant *Staphylococcus aureus* (MRSA), vancomycin resistant *Enterococcus* (VRE), extended spectrum beta-lactamase (ESBL) producing enterobacteriaceae, and multidrug resistant Gram-negative bacilli. These bacteria occur frequently on ICUs [27–29] and BICUs [11,20,22,23,25,26,28]. The Swedish strategic program against antibiotic resistance (STRAMA), which started in 1994 reported recently that invasive infections caused by ESBL-producing *E. coli* and *Klebsiella* spp. have increased also in Sweden, but the proportion of pathogens resistant to 3rd generation cephalosporins causing invasive infections is still rather low from the European and international perspective [32]. Scandinavian countries and the Netherlands have been more successful in ''search and destroy'' actions against MRSA. The incidence of MRSA in Sweden is approximately 1% among invasive isolates compared to a 20-fold higher mean incidence in European countries [32]. Within ICU-Strama we have surveyed distribution of microbial species, and antimicrobial resistance (AMR), in isolates from patients admitted to the Burn Center at Linköping University Hospital, Sweden, from 1994 through 2012.

2. Aim

The aim of this study was to investigate the antibiotic consumption pressure and resistance rates in a Swedish burn unit.

3. Materials and methods

Setting: The Burn Center, Department of Hand-, Plastic-, and Burn Surgery, University Hospital of Linköping, Sweden. This is one of two national burn centers and has a catchment population of approximately 4.5 million inhabitants.

Patient data: Data were collected from patient records at the Burn Center in Linköping from April 1st 1994 through December 31st 2012. The following patient data were collected and aggregated: admission, discharge, age, gender, mean % total body surface area (TBSA%), mortality, number of admission days on ventilator, and number of admission days on dialysis.

Microbiological data acquisition: A search of the database of the Department of Clinical Microbiology Laboratory, University Hospital of Linköping was performed, looking for positive bacterial and yeast cultures of samples taken from all sources, in patients admitted to the Burn Center between April 1st 1994 and December 31st 2012. Data on species and antimicrobial susceptibility were entered into a secondary database. Only initial isolates of bacteria and yeasts were considered, and thus repeat isolates of the same species and with the same antibiogram from the same patient were excluded.

Microbiological cultures: All samples were taken on clinical indication from burn wound surfaces, tracheal secretions, intraluminal catheters, urine, and blood using conventional culture techniques. Microbiology diagnostics including species determination of all isolates were performed at the Clinical Microbiology Laboratory, University Hospital of Linköping. Data are presented here as ''all samples'' or ''blood samples''. Trend analysis was performed for the whole study period.

Susceptibility testing and breakpoints: Susceptibility testing was performed at the Clinical Microbiology Laboratory, University Hospital of Linköping, according to the Swedish Reference Group for Antibiotics (SRGA) from 1994 to 1999 and the European Committee on Antimicrobial Susceptibility Testing (EUCAST) from 1999 until 2012 [33]. Antibiotic resistance was interpreted as susceptible (S), intermediate (I), or resistant (R). Decreased susceptibility was defined as the sum of I and R. *E. coli* and *Klebsiella* spp. ESBL-phenotype was defined as resistant to 3rd generation cephalosporins (cefotaxime). No major changes in breakpoints have been made for species-antibiotic combinations that affect the susceptibility testing results.

Antibiotic consumption: Sales statistics on antibiotic consumption at the Burn Center were collected. These figures were based on the anatomical therapeutic chemical (ATC) classification system and were obtained from the County of Östergötland Pharmacy Department, Sweden. Antibiotic consumption was expressed as defined daily doses (DDD) per 1000 occupied bed days (DDD/TAD). We used the annually updated DDD as calculated using the WHO Collaborating Centre for Drug Statistics Methodology; the average maintenance dose per day in adults for the main indication of the drug [34].

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Ethical approval: Ethical approval was waived since this was a quality assurance project within ICU-Strama. No intervention was involved and only aggregated data were considered.

Statistical analysis: Linear regression and correlation were calculated using Statistica for PC (Ver. 10. Stat Soft Inc., Tulsa, OK, USA). Exact logistic regression for resistance data and one-way ANOVA with *post hoc* Bonferroni correction for DDD data was performed using Stata SE for mac OS (Version 12.0 StataCorp, College Station, TX, USA). Logistic regression: resistance/not resistance was used as dependent variable and year was used as independent variable. OR >2.0 or <0.5, CI lower and upper limit <1 or >1 were considered statistically significant.

Data are presented as mean ± Standard Deviation (range) if not otherwise stated. Probabilities are two-sided and a $p < 0.05$ was considered statistically significant. Output is displayed as percentage chance of resistance in isolates and number of positive isolates over time.

4. Results

4.1. Clinical data (Table 1)

During the study period a total of 1570 burn patients were treated at the Linköping Burn Center (57–152 patients per year). There was an annual mean TBSA% (dermal and full-thickness burns) of 13.4% (range 9.5–18.5). The annual mean mortality rate was 5.4% with a median of 4 patients each year. The number of days on ventilator was 10.8% of all admission days, and the corresponding figure for dialysis was 0.3%. The percentage of patients on mechanical ventilation decreased significantly during the study. Mean TBSA% was positively correlated to the annual mortality rate.

4.2. Microbial isolates from all sources (Table 2)

A total of 15,006 microbial samples (blood, wound, other body fluids, or catheters) were taken and recorded in the laboratory IT system. Of all microbial samples, 4531 were positive (30.2%). Positive cultures consisted of Gram-positive (2689 isolates, 59.3%), Gram-negative (1122 isolates, 24.8%), *Candida* spp. (178, 3.9%), and samples of non-specified species (542, 12.0%). The average number of isolates per year was for: Gram-positive spp. 141.5 ± 85.6 (77–372), Gram-negative spp. 59.1 ± 23.8 (28–100), and *Candida* spp. 9.4 ± 4.9 (5–22). A mean of 2.82 (1.59–4.64) positive isolates per patient per year was obtained of which 1.64 (0.93–2.9) were Gram-positive, 0.72 (0.41–1.1) Gram-negative, and 0.11 (0.048–0.21) *Candida* spp.

There was a statistically significant decrease in Gram-negative bacteria, but not a correspondingly significant increase in *Candida* spp. and Gram-positive bacteria. The most frequently isolated species were coagulase-negative staphylococci (CoNS) (20.3%), followed by *S. aureus* (19.1%), *Enterococcus* spp. (10.0%), *Streptococcus* spp. (10.0%), *Pseudomonas aeruginosa* (4.6%), *Candida* spp. (3.9%), and Enterobacteriaceae (15.6%) including *Enterobacter* spp. (5.3%) and *Escherichia coli* (3.8%). These nine species made up for approximately 83.5% of all positive isolates.

Gram-positive bacteria: *S. aureus*, *Streptococcus agalactiae*, and *Enterococcus faecalis* increased significantly during the study period, whereas *Streptococcus pneumoniae* and *Streptococcus pyogenes* decreased significantly.

Gram-negative bacteria: Enterobacteriaceae formed the largest group followed by non-fermentative Gram-negative bacteria including *P. aeruginosa* and *Acinetobacter* spp. Non-fermentative Gram-negative bacteria including *Acinetobacter* spp., Enterobacteriaceae (including *Enterobacter* spp.), and *Moraxella catarrhalis* all showed significant decreases.

4.3. Blood isolates (Table 3)

During the study period a total of 2236 blood samples were taken and recorded in the laboratory IT system. Of these 416 (18.6%) were positive; Gram-positive bacteremia (157, 37.8%), Gram-negative bacteremia (161, 38.7%), and Candidemia (32, 7.7%). The most frequently found organisms were: CoNS (27.4%, 2.6/TAD); Enterobacteriaceae (20.7%, 2.0/TAD) including *E. coli* (2.4%, 0.2/TAD); *Streptococcus* spp. (13.9%, 0.28/TAD); *Enterococcus* spp. (13.9%, 1.3/TAD); *Candida* spp. (7.7%, 0.7/TAD); *S. aureus* (7.5%, 0.7/TAD); and non-fermentative gram-negative

Table 1 – Clinical data of burn patients. Grouped into four-year periods* from 1994 to 2012.

Year	1994–1997	1998–2001	2002–2005	2006–2009	2010–2012 (3 y)	*p*	Trend[a]
Patients admitted, *N*	324	273	318	264	391	0.07	
Deceased, *N* (%)	15 (4.6)	14 (5.1)	27 (8.5)	14 (5.3)	9 (2.3)	0.89 (0.66)	
Children <age 16, *N* (%)	124 (38)	104 (38)	111 (34)	92 (34)	119 (30)	(0.12)	
Mean TBSA (%)	13.6	14.6	14.8	12.6	10.7	0.07	
Mean LOS, days	31.8	26.6	25.9	30	25.4	0.65	
LOS/TBSA%	2.3	1.8	1.8	2.4	2.4	0.32	
Patients on Ventilator, *N* (%)	81 (25)	74 (27)	72 (23)	36 (14)	69 (18)	(0.02)	(−0.72)
Ventilator days (%)	815 (8)	699 (10)	1062 (13)	999 (12)	1132 (11)	0.11	
Patients on Dialysis, *N* (%)	4 (1)	1 (0.4)	2 (0.6)	9 (3)	3 (0.8)	(0.32)	
Dialysis days (%)	61 (0.6)	12 (0.2)	12 (0.1)	41 (0.5)	20 (0.2)	0.88	
Total admission days (TAD)	10,292	7254	8226	7916	9919	0.27	

[a] Regression coefficient is displayed. Trends were calculated through linear regression and displayed in percentage unit increase or decrease per year.

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Table 2 – Isolates from all cultures 1994–2012.

Group/Species	n	%*	Range (%)	p	Trend[a]
Enterobacteriaceae	**716**	15.8	11–22	0.035*	−0.24
Enterobacter spp.	239	5.3	2.4–11	0.023*	−0.23
Escherichia coli	170	3.8	1.3–5.5	0.054	
Klebsiella spp.	134	3.0	1.4–5.2	0.077	
Proteus spp.	73	1.6	0.0–3.2	0.23	
Serratia spp.	57	1.3	0.0–4.3	0.278	
Citrobacter spp.	34	0.8	0.0–2.3	0.70	
Morganella morganii	9	0.2	0.0–1.2	0.77	
Non-fermentative Gram-neg	**324**	7.2	3.9–14	0.013*	−0.30
Pseudomonas aeruginosa	209	4.6	2.0–9.8	0.19	
Acinetobacter spp.	64	1.4	0.0–3.6	0.032*	−0.09
Stenotrophomonas maltophilia	51	1.1	0.0–3.7	0.074	
Staphylococcus aureus	866	19.1	11–27	0.0002*	+0.65
Coagulase-negative staphylococci (CoNS)	921	20.3	14–25	0.155	
Streptococcus spp.	**451**	10	3.6–15	0.031*	−0.29
Streptococcus agalactiae	53	1.2	0.0–2.1	0.0038*	+0.07
Streptococcus pneumoniae	47	1.0	0.0–3.7	0.0049*	−0.11
Streptococcus pyogenes	45	1.0	0.0–2.6	0.031*	−0.08
Enterococcus spp.	**451**	10	5.5–15	0.069	
Enterococcus faecium	274	6.0	0.4–6.0	0.24	
Enterococcus faecalis	110	2.4	0.7–8.5	0.0003*	+0.34
Candida spp.	**168**	3.7	2.3–6.0	0.070	
Candida albicans	140	3.1	0.8–6.0	0.93	
Other					
Moraxella catarrhalis	38	0.8	0.0–3.2	0.0025*	−0.12
Haemophilus influenzae	29	0.6	0.0–2.3	0.44	
Bacteroides spp.	15	0.3	0.0–1.5	0.22	
Total positive cultures	**4531**				

* Percentage species were calculated from total positive cultures pooled for all years.
[a] Regression coefficient is displayed. Trends were calculated through linear regression and displayed in percentage unit increase or decrease per year.

Table 3 – Blood isolates 1994–2012.

Category/Species	n	%*	Range (%)	p	Trend[a]
Enterobacteriaceae	**86**	20.7	6.7–44	0.39	
Enterobacter spp.	31	7.5	0.0–25	0.38	
Serratia spp.	19	4.6	0.0–22	0.41	
Klebsiella spp.	17	4.1	0.0–10	0.35	
Escherichia coli	10	2.4	0.0–7.5	0.90	
Citrobacter spp.	4	0.96	0.0–5	0.12	
Proteus spp.	3	0.7	0.0–5.9	0.83	
Morganella morganii	2	0.48	0.0–4.8	0.82	
Non-fermentative Gram-neg	**22**	5.3	0.0–18	0.21	
Pseudomonas aeruginosa	13	3.1	0.0–13	0.42	
Stenotrophomonas maltophilia	6	1.4	0.0–9.1	0.35	
Acinetobacter spp.	3	0.7	0.0–9.1	0.017*	−0.05
Staphylococcus aureus	31	7.5	0.0–24	0.84	
Coagulase Negative Staphylococci; CoNS	114	27.4	14–55	0.14	
Streptococcus spp.	**12**	2.9	0.0–10	0.68	
Enterococcus spp.	**58**	13.9	0.0–28	0.16	
Enterococcus faecalis	34	8.2	0.0–20	0.20	
Enterococcus faecium	21	5.0	0.0–13	0.13	
Candida spp.	**32**	7.7	0.0–18	0.23	
Candida albicans	23	5.5	0.0–13	0.45	
Other					
Moraxella catarrhalis	1	0.24	0.0–4.3	0.48	
Bacteroides spp.	2	0.48	0.0–4.5	0.18	
All	**416**				

* Percentage species were calculated from total positive cultures pooled all the years.
[a] Regression coefficient is displayed. Trends were calculated through linear regression and displayed in percentage unit increase or decrease per year.

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Table 4 – Antibiotic resistance (I + R) for the most common species 1994–2012 on all samples.

Species	Type	*n*	%[b]	OR	CI[c]	Trend[a]
Escherichia coli	Ampicillin	55	93%	0.93	0.78–1.11	
	TMP/SMX	39	26%	1.07	1–1.15	
	Quinolones	23	15%	1.14	1.04–1.28*	+0.13
	Cefotaxime (ESBL)	13	8%	1	0.91–1.1	
	TZP	16	11%	1.01	0.93–1.11	
	Imipenem	1	1%	0.53	0.02–1.11	
	Aminoglycosides	6	5%	1.59	0.98–3.41	
Enterobacter spp.	Cefotaxime	64	27%	1.01	0.96–1.06	
	TZP	48	22%	0.95	0.86–1.04	
	Quinolones	51	22%	0.96	0.91–1.02	
	TMP/SMX	43	20%	0.98	0.92–1.03	
	Aminoglycosides	10	8%	0.93	0.81–1.08	
	Imipenem	4	2%	1.03	0.87–1.24	
Klebsiella spp.	Quinolones	13	10%	1.03	0.94–1.14	
	TZP	13	10%	0.95	0.86–1.04	
	Cefotaxime (ESBL)	6	5%	1	0.87–1.15	
	TMP/SMX	5	4%	1.15	0.97–1.46	
	Aminoglycosides	4	5%	1.2	0.9–1.94	
	Imipenem	0	0%			
Acinetobacter spp.	Ceftazidime	19	73%	0.96	0.78–1.17	
	TZP	23	53%	1	0.88–1.14	
	Quinolones	10	15%	0.72	0.5–0.9*	−0.33
	TMP/SMX	7	11%	0.79	0.59–0.95*	−0.24
	Aminoglycosides	1	3%	1.77	0.51–47.79	
	Imipenem	2	3%	1	0.78–1.29	
P. aeruginosa	Imipenem	56	26%	1.03	0.98–1.09	
	TZP	52	24%	0.99	0.93–1.04	
	Quinolones	49	23%	1.03	0.97–1.09	
	Ceftazidime	30	15%	1.01	0.94–1.08	
	Aminoglycosides	2	1%	0.43	0.06–0.96*	−0.86
S. aureus	Fucidic acid	72	8%	0.98	0.94–1.03	
	Clindamycin	37	4%	1.11	1.03–1.2*	+0.10
	Oxacillin (MRSA)	15	2%	1.08	0.98–1.21	
	Aminoglycosides	11	2%	1.35	0.99–2.08	
	Rifampicin	3	0%	1.19	0.91–1.91	
	Vancomycin	0	0%			
CoNS	Oxacillin	489	52%	1.03	0–inf	
	Fucidic acid	434	44%	1	0.98–inf	
	Clindamycin	391	44%	1.01	0.99–1.03	
	Aminoglycosides	342	35%	0.94	0.88–1	
	Rifampicin	96	11%	1.02	0.98–1.06	
	Vancomycin	0	0%			

[a]Trend is logistic regression coefficient.
[b] Percentage Intermediary (I) and Resistant (R) samples were calculated on total samples per species per antibiotic pooled for all study years.
[c] 95% confidence interval, lower and upper limit in logistic regression.
* Significant odds ratio; Logistic regression: resistance/not resistance was used as dependent variable and year was used as independent variable. A 95% confidence interval not including one was significant.

species (5.3%, 0.5/TAD) including *P. aeruginosa* (3.1%, 0.3/TAD). Only *Acinetobacter* spp. showed a significant decrease over the study period.

4.4. *Susceptibility to antibiotics (Table 4)*

The following species had a statistical significant change in suscetibility: *Escherichia coli*: increased resistance to quinolones (OR 1.14), *Acinetobacter* spp: decreased resistance to quinolones (OR 0.72) and TMP/SMX (OR 0.79), *P. aeruginosa*: decreased resistance to aminoglycosides (OR 0.43), and *S. aureus:* increased resistance to clindamycin (OR 1.11).

4.5. *Percent of isolates non-susceptible to various antibiotics*

Escherichia coli: Highest resistance was seen for ampicillin (93%) followed by trimethoprim/sulfamethoxazole (TMP/SMX) (26%) and quinolones (15%), piperacillin/tazobactam (TZP) (11%) and cefotaxime (ESBL phenotype) (8%). Low resistance levels were seen for imipenem (1%) and aminoglycosides (5%).

***Enterobacter* spp.**: High levels of resistance to cefotaxime (27%), TZP (22%), quinolones (22%), and TMP/SMX (20%). Aminoglycosides (8%) and imipenem (2%) showed low resistance levels.

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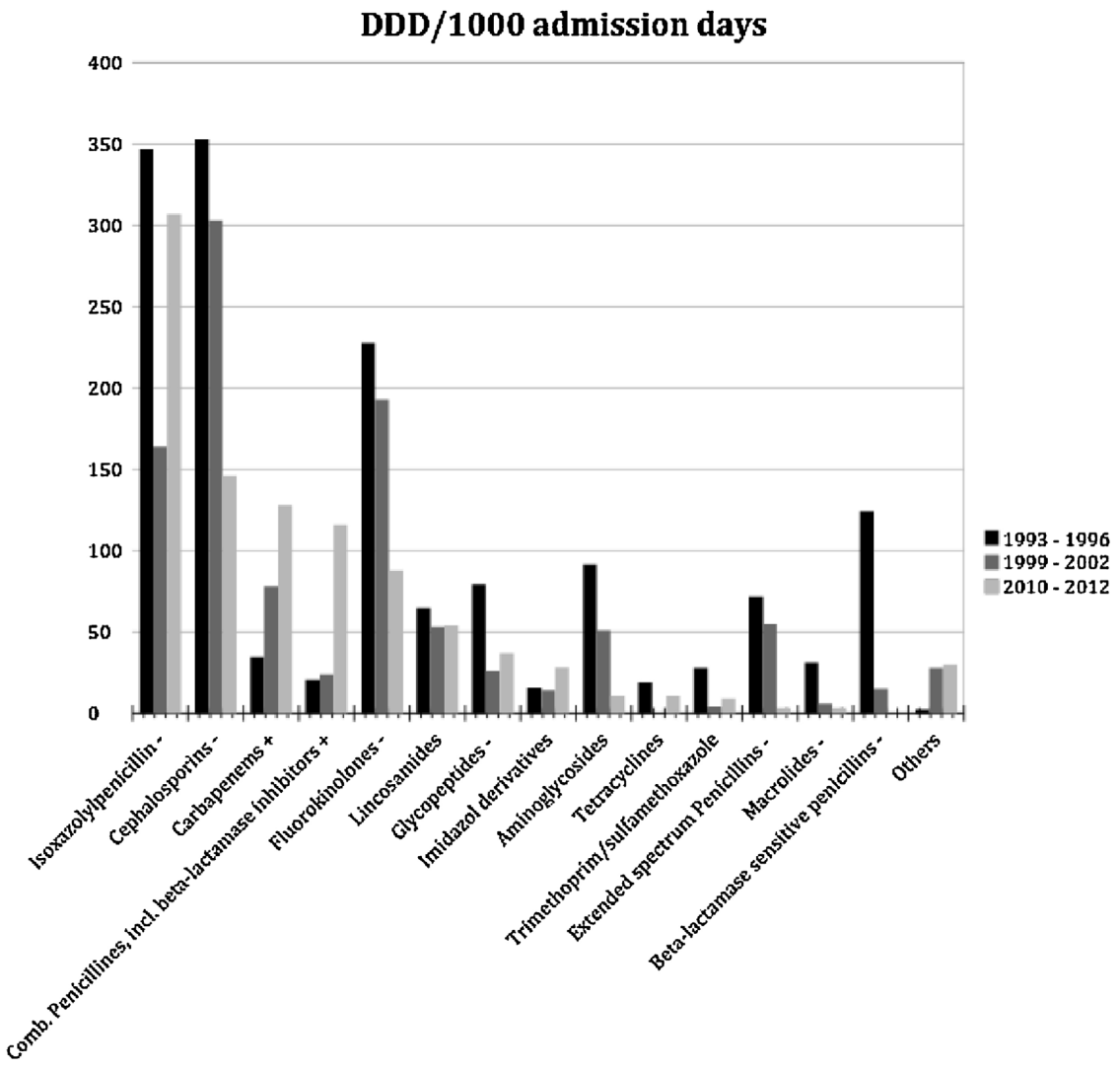

Fig. 1 – DDD antibiotics data per 1000 admission days for years 1993–1996, 1999–2002 and 2010–2012. "+" marks statistical significant increase and "-" marks statistical significant decrease.

***Klebsiella* spp.:** High resistance levels (10%) were seen for quinolones and TZP. The resistance to cefotaxime (ESBL phenotype) was (5%) and low resistance levels were seen for aminoglycosides (5%), TMP/SMX (4%). No resistance toward imipenem was found.

***Acinetobacter* spp.**: High levels of resistance toward ceftazidime (73%), TZP (53%), quinolones (15%) and TMP/SMX (11%). The aminoglycoside and imipenem resistance levels were low (3%).

P. aeruginosa: High levels of resistance to imipenem (26%), TZP (24%) and quinolones (23%) and slightly lower resistance to ceftazidime (15%). *P. aeruginosa* showed low (1%) resistance to aminoglycosides.

S. aureus: Low resistance levels to fucidic acid (8%), aminoglycosides (2%), and full susceptibility to rifampicin and vancomycin. *S. aureus* showed low (4%) resistance to clindamycin and only 2% were oxacillin resistant (MRSA).

CoNS: High levels of resistance to oxacillin (52%), fucidic acid (44%), clindamycin (44%), and high resistance to aminoglycosides (35%). Lower resistance levels were seen for rifampicin (11%) and no resistance to vancomycin.

4.6. *Resistance of major clinical importance*

Of 866 patients infected or colonized with *S. aureus*, 15 were MRSA positive (1.7%) which corresponds to 0.34/TAD. Corresponding figures for resistance to 3rd generation cephalosporins (ESBL phenotype) were for *E. coli* (8%) and *Klebsiella* spp. (5%), corresponding to 0.3/TAD and 0.14/TAD respectively. Carbapenem resistance (which was introduced before the study started) was found in 26% of all cultures of *P. aeruginosa* representing 1.28/TAD. No VRE cases were found.

4.7. *Antibiotic consumption*

Consumption of antibiotics for three periods; 1993–1996, 1999–2002 and 2010–2012 is shown in Fig. 1. During 1993–1996 was the yearly mean antibiotic consumption 1510 DDD/1000 admissions and the corresponding figure was the following two periods 1014 and 971 respectively. Isoxazolylpenicillin, cephalosporins, quinolones and glycopeptides decreased

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whereas carbapenems and piperacillin/amoxicillin + beta-lactamase inhibitors increased during the study.

During 2010–2012, narrow spectrum anti-staphylococcal penicillin (isoxazolylpenicillin) was the most commonly prescribed antibiotic, followed by cephalosporins, carbapenems, piperacillin/amoxicillin + beta-lactamase inhibitors and quinolones.

5. Discussion

There was an annual mean TBSA% (dermal and full-thickness burns) of 13.4% (range 9.5–18.5) and an annual mean mortality rate of 5.4%. The mortality rate was similar to a study by Hranjec et al. showing 4% mortality rate but with a mean TBSA% of only 4.4% [35]. Edelman et al. also showed low (3.8%) mortality [36], but Brusselaer et al. showed 15% mortality rate with 34% median TBSA% [4]. Patel et al. showed 3% mortality rate with 40% mean TBSA% [9]. Due to the lack of TBSA% risk adjustment reports on mortality, these differences must be interpreted with caution.

Septicemia and Gram-negative bacterial infections are the main causes of morbidity and mortality in burn patients [4,7–9]. However, no such correlation to mortality was shown in our study. SRGA and EUCAST breakpoints and methodologies have been used throughout the study and these have been stable and conservative [33]. Overall, no indications of increased infectious rate was seen. This is also supported by the fact that the total antibiotic subscriptions did not increase.

Coagulase-negative staphylococci were the most frequently isolated microorganisms in this study. Similar results have been seen in other studies [20,22,25,37]. CoNS is considered a microbe of low virulence but may be a significant pathogen in central line bloodstream infections also in burn patients [38]. A considerably high resistance toward quinolones was shown with a mean of 50% resistance (data not shown). This is in line with the general increase in resistance toward ciprofloxacin found in other studies [20,22,26].

***Candida* spp.** are harmless saprophytes as long as they only colonize the burn wound. When invading viable subeschar tissue or the blood stream they become dangerous pathogens with a mortality rate exceeding 90% [39,40]. It has been shown that patients with *Candida* spp. infections are more likely to have received broad spectrum antibiotics *e.g.* imipenem, vancomycin, and aminoglycosides [41]. This study was not designed to measure risk factors for candida infections but 7.7% of all blood isolates were *Candida* spp. Some studies show *Candida* spp. to be an important cause of clinical complications [42–44], while others have shown no significant increase in mortality [45].

S. aureus was a predominant microbe in the skin flora and constituted 19.6% of all isolates and 7.5% of blood isolates. There was a stable low (<2%) MRSA rate and the only significant increased resistance found was to clindamycin.

***Enterococcae* spp**. are normal constituents of the gastrointestinal tract but may colonize wounds in hospitalized patients [46], especially in (B)ICU patients as a result of gastrointestinal translocation [47,48]. Enterococcal infections have been associated with increased morbidity and mortality [23,49,50] but this could not be studied in our Burn center due to very low mortality. There was a significant increase of *Enterococcus faecalis* but not a single case of VRE was observed.

Enterobacteriaceae: Resistance against 3rd generation cephalosporins, imipenem, and aminoglycosides among *Enterobacter* spp were 27.2% and 8% respectively. Corresponding figures for *E. coli* were 8, 1, 5%, and *Klebsiella* spp. 5, 0, 5%. The only significant change was an increase in resistance among *E. coli* toward quinolones (15%).

***P. aeruginosa*'s** Carbapenem resistance (which was introduced before the study started) was found in 26% of all cultures of *P. aeruginosa* but represented only 1.28/TAD, since *P. aeruginosa* only constituted 4.6% of all isolates. Hence, the risk for *P. aeruginosa* resistance was low compared to other centers reporting a predominance of *P. aeruginosa* infections and being the dominant species in Gram-negative infections [10,11,23,28]. One report indicated a decrease in burn wound colonization with *P. aeruginosa* [52], which was not the case in our study. *P. aeruginosa* in the blood stream has been suggested to be related to overall mortality [9].

5.1. *Resistance of major clinical importance in comparison*

The frequencies of MRSA (2%) and ESBL-producing Enterobacteriacae (5–8%) were low but the frequency of carbapenem-resistant *P. aeruginosa* (26%) was high. Guggenheim et al. reported an increase in MRSA infections from 3% to 13% during 1994–2005. Their numbers of ESBL-producing *Klebsiella* spp. (2% rising to 20%) were also higher compared to our findings. ESBL-producing *E. coli* from Guggenheim's study showed increased resistance from 1% to 3–4% compared to 8% in our study. *P. aeruginosa* resistance to imipenem was also increased from 12% to 27% compared to 26% in our study [22]. Keen et al. showed a high multidrug resistance among *Klebsiella* spp. (17%), *P. aeruginosa* (15%) and 34% of the *S. aureus* strains isolated were classified as MRSA [53]. In a study by Song et al. from Seoul, South Korea, MRSA levels were as high as 98% of all positive samples and resistant *P. aeruginosa* was found in 52% of the isolates [25].

5.2. *Antibiotic consumption*

Data on antibiotic consumption are very scarce in reports from other burn units and thus cannot be compared. One limitation of measuring DDDs is that doses for individual patients and patient groups will often differ from the DDD since they are based on, and adjusted to, individual characteristics (age, weight, source of infection, renal function, *etc.*). However DDD/TAD still describes the most commonly used antibiotics at our burn center which is narrow spectrum anti-staphylococcal penicillin (isoxazolyl penicillin). We still have low MRSA rate (1.7%) and the use of glycopeptides was low. The antimicrobial resistance has remained low among gram-positive pathogens in our unit and this is probably an effect of low inflow of antibiotic resistant gram-positive bacteria from the society but also sufficient infection control measures within the burn center. We found a rather high level of resistance among gram-negative pathogens which may explain increasing use of piperacillin-tazobactam as well as carbapenems.

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5.3. Study limitations

Data regarding the records of individual patients and their relationship to microorganism species, antibiotic treatment, resistance, or changes in antibiotic treatment were not collected. Details as to when the samples were taken were not included; neither did we include specific information on antibiotic resistance of isolates from blood cultures since the low number of positive blood cultures prevented any further statistical analysis. Furthermore, no data on simultaneous multiple microbial infections and multiple antibiotic treatments in the same patient were available.

5.4. Future perspectives

Despite many advances in the treatment of burns, infection remains a major concern in burn units. Strict hygiene routines, minimal catheterization and ventilator times, up-to-date topical burn wound care, strict antibiotic treatment algorithms, close monitoring of the burn unit's microbial flora, an understanding of the patients' endogenous bacteriologic spectrum, and excellent intensive care are important if we are not to lose the battle against antibiotic resistance and decrease mortality and morbidity [15,25,35,54,55].

5.5. Main findings

The study showed that the risk for infection or colonization with antibiotic resistant bacteria was low: 0.34/TAD for MRSA, 0.3/TAD for *E. coli* resistant to 3rd generation cephalosporins (ESBL phenotype), 0.14/TAD for *Klebsiella* spp. ESBL phenotype, 1.28/TAD for carbapenem resistant *P. aeruginosa* and 0.04/TAD for carbapenem resistant *Acinetobacter* spp. This is similar to other burn units in the developed world [20–26,28,53].

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Appendix A. Supplementary data

Supplementary data associated with this article can be found, in the online version, at http://dx.doi.org/10.1016/j.burns.2016.01.025.

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