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Increase in bloodstream infections in Finland, 1995–2002

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SUMMARY

A national, population-based laboratory surveillance of bloodstream infections (BSI) in Finland was performed. Blood-culturing rates were determined from data from clinical microbiology laboratories and trends in rates were evaluated using Poisson regression. During 1995–2002, 51 510 cases of BSI were notified; the annual incidence increased from 104 to145 cases/100 000 (40 %). Rates increased in all age groups but persons aged ⩾75 years accounted for 28 % of cases and showed the largest rate increase. *Escherichia coli*, coagulase-negative staphylococci, *Staphylococcus aureus* and *Streptococcus pneumoniae* accounted for 58 % of isolates and their relative proportions were unchanged over time. The annual blood-culturing rate increased by one-third during the study period but the number of BSI detected per blood cultures remained unchanged. Regional BSI incidence was significantly associated with blood-culturing rates. We conclude that the increase in BSI rates may have been due to more frequent blood culturing but was not associated with changes in the reporting system or aetiology of BSI.

INTRODUCTION

Bloodstream infections (BSI) are associated with high morbidity and mortality. Surveillance of these infections provides important information for developing therapeutic guidelines and prevention strategies. Few population-based studies of BSI are available [1] and most surveillance reports are based on the experience of a single hospital or a selection of hospitals, single pathogens or either nosocomial or community-acquired cases [2, 3].

An increase in the incidence of BSI and sepsis was observed in England and in the United States in the 1990s [1, 4]. Possible reasons for this may include ageing of the population and an increased prevalence of risk factors for BSI such as invasive procedures, underlying illness, immunocompromising conditions and increased survival of severely ill patients. The use of national computer-based registries for complete and rapid reporting of communicable diseases with electronic laboratory-based systems is increasing [1, 5]. In Finland, a nationwide registry with laboratory-based reporting for communicable diseases including all BSI was implemented in 1995. At the beginning most of the BSI cases were reported via mail, but electronic reporting has increased gradually during the years.

We investigated population-based rates, trends and regional variation in BSI reported to the national registry. Rates of blood culturing were evaluated by surveying all clinical microbiology laboratories performing blood cultures in Finland.

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MATERIALS AND METHODS

Population-based surveillance

In 2002, the population of Finland was 5·2 million. The national health-care system is organized into 20 geographically and administratively defined health-care districts, with catchment populations ranging from 0·07 to 1·42 million. Five of the health-care districts have university hospitals with tertiary care reference functions. In 1995, laboratory-based national surveillance for communicable diseases began in Finland and all clinical microbiology laboratories are required to notify all bacterial and fungal blood-culture isolations to the National Infectious Disease Register (NIDR) maintained by the National Public Health Institute. The laboratories report either electronically directly from the laboratory database to the NIDR database or via mail. Each notification contains the following information: date when specimen was obtained, isolated microbe, patient's date of birth, gender, treatment location, reporting laboratory and the method of reporting (electronic or via mail).

Case definition

A case of BSI was defined as a patient from whom a bacterial species or fungus was isolated from blood culture and reported to the NIDR during 1995–2002. Duplicate notifications were merged into a single case if they occurred within 3 months of each other.

Survey of blood-culturing practices

Information on the annual numbers of blood-culture sets processed during the years 1995–2002 was requested from all ($n=31$) clinical microbiology laboratories reporting BSI to the NIDR, all of which were licensed to perform blood cultures, involving compulsory participation in external quality assurance schemes. The response rate in the survey was 100%.

Statistical analysis and calculation of incidence rates

Data from the National Population Information System were used as denominators to calculate age- and sex-specific incidence rates as well as rates of blood-culture sampling. The average annualized incidence rates during the study period were calculated by using the total number of cases and population during 1995–2002. For male:female incidence rate ratios (RR), 95% confidence intervals (CI) were calculated. Categorical variables were analysed with the χ^2 test, using Yates' correction. To evaluate secular trends, age- and sex-specific rates were calculated for each 12-month period from January 1995 to December 2002. A Poisson regression model was used to assess whether the observed changes in the rates were statistically significant. Spearman correlation coefficients (and P values) were calculated to assess the relation between regional BSI rates and the rates of blood cultures processed. To evaluate whether a change from mail to electronic reporting method in the health district during the study period was associated with the BSI rate, the data were divided in half for the year during which the reporting method changed (year 0). Years before and after year 0 were numbered from -6 to $+6$. Poisson regression was used to compare trends in the annual BSI rates during the years before and after the reporting change. Data were analysed by using SPSS for Windows, version 12.0 (SPSS Software, Chicago, IL, USA).

RESULTS

During 1995–2002, a total of 51 510 cases of bacterial or fungal BSI were reported to the NIDR; the average annualized incidence was 125 cases/100 000 population. Fifteen categories of microbes accounted for 89% of all cases; *Escherichia coli*, coagulase-negative staphylococci, *Staphylococcus* (*Staph.*) *aureus*, and *Streptococcus pneumoniae* were the four most common species, accounting for 58% of the cases. Only minor variations were observed in the annual proportions of Gram-positive bacteria (from 52% to 55%), Gram-negative bacteria (from 46% to 43%), fungi (from 1·7% to 2·0%) and anaerobic bacteria (from 6·4% to 5·2%). Each year, the proportion of the most common categories of microbes remained unchanged during the study period with ranges for *E. coli* of 23–25%, coagulase-negative staphylococci 11–13%, *Staph. aureus* 12–13%, and *S. pneumoniae* 8–9%) (Fig. 1). The annual proportion of potentially colonizing bacteria (coagulase-negative staphylococci, *Micrococcus* spp., *Propionibacterium* spp., *Corynebacterium* spp., and *Bacillus* spp.) did not change (13–15%).

The median age of cases was 64 years (range 0–102 years); 28% were aged $\geqslant$75 years. The incidence of BSI was highest among infants and the elderly

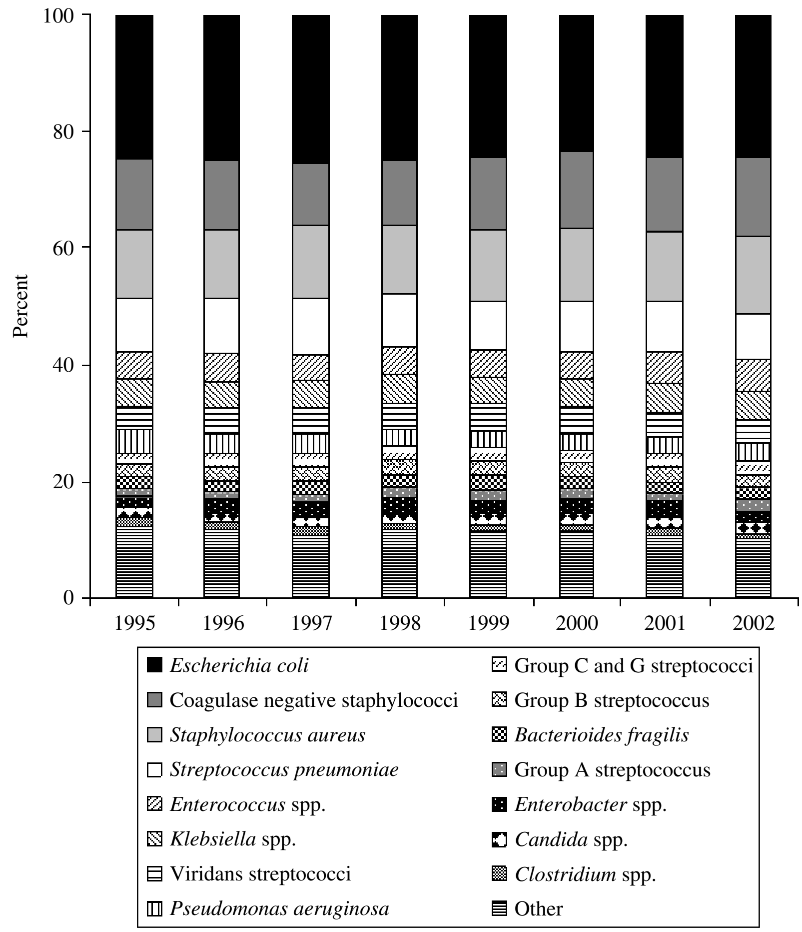

Fig. 1. Annual distribution of pathogens causing bloodstream infections, Finland, 1995–2002.

(Table 1) and the BSI rate was higher among males than females (RR 1·1, 95% CI 1·1–1·2). The male:female RR for age groups aged ⩾45 years varied between 1·5 and 1·6. The annual number of BSI cases increased from 5275 in 1995 to 7503 in 2002. The incidence increased by 40%, from 104 to 145 cases/100 000 population (Fig. 2, $P<0{\cdot}001$). Significant increases in the annual rates were observed in all age groups, except in the 1–14 years age group (Table 1). The magnitude of the change ranged from 19% to 41% by age group with the largest increase in persons aged ⩾75 years (from 441 to 622/100 000 population). Increases in rates were observed in both genders (Tables 1–3). The national average annual rate of blood cultures performed was 3209/100 000 population during the study period. From 1995 to 2002, the annual rate of blood cultures performed increased by 33%, from 2766 to 3685/100 000 (Fig. 2). However, the proportion of BSI cases per cultures performed did not change (range 37–42/1000 cultures per year).

The average annual BSI rate varied regionally by approximately twofold, from 90 to 187 cases/100 000 population (Table 4). Of all notified cases, 59% were reported from the five largest health-care districts, in which tertiary care university hospitals were located. The BSI incidence was higher in these five districts than in the 15 other districts (133 *vs.* 116/100 000 population, $P<0{\cdot}001$). The annual rate of blood cultures performed varied from 2053 to 4900/100 000 population by health-care district (Table 2) and it was associated with the BSI rate (Spearman correlation coefficient 0·82, $P<0{\cdot}001$). The yield for blood cultures was 39 BSI cases/1000 blood cultures performed (range by health-care districts, 28–47). The increase in the annual BSI incidence ranged from 10% to 101% by health-care district and rate increases were similar in districts that had a university hospital compared with other districts (36%, from 111 to 150/100 000 population *vs.* 45%, from 94 to 136/100 000 population).

Table 1. *Annual incidence of bloodstream infection (BSI) by age in Finland, 1995–2002*

Age group (years)	Annual incidence (cases per 100 000) 1995	1996	1997	1998	1999	2000	2001	2002	1995–2002	Change (%)*	*P* value
<1	427	404	385	490	524	479	485	569	469	33	<0·001
1–14	30	30	33	30	34	35	29	36	32	19	0·055
15–24	27	30	30	31	37	36	46	35	34	29	<0·001
25–34	39	38	42	46	49	46	48	51	45	31	<0·001
35–44	46	55	57	52	59	62	68	59	57	29	<0·001
45–54	80	81	96	97	96	104	109	110	97	38	<0·001
55–64	145	148	167	172	185	184	189	191	174	32	<0·001
65–74	290	297	313	296	323	336	352	354	320	22	<0·001
⩾75	441	504	510	501	518	580	642	622	543	41	<0·001
All	104	111	118	118	127	134	144	145	125	40	<0·001

* Change in rate from 1995 to 2002.

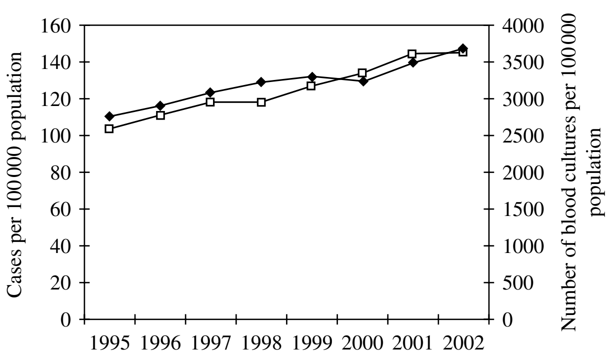

Fig. 2. Annual incidence of bloodstream infections (□), and rate of blood culture sampling (◆), Finland, 1995–2002.

The annual proportion of electronically reported BSI cases increased from 4% to 80% and of the 20 health-care districts, 12 changed from paper reports to electronic reporting during the study period. These 12 districts accounted for 82% of all cases reported. The increase in BSI incidence was lower in these districts than in the eight other districts which reported via mail during the whole study period (average annual increase: 4·6%, 95% CI 4·1–5·0 *vs.* 7·2%, 95% CI 6·2–8·1; $P<0·001$). In the 12 health-care districts that changed their reporting method during the study, the change to electronic reporting did not affect the overall trend in BSI rates. The annual increase between the years −1 to 0 (4·7%) and 0 to +1 years (4·6%) were within the 95% confidence interval of the average annual increase (4·1–5·0%). After the year +1 the average annual increase was similar to before the year −1 (3·7%, 95% CI 2·4–4·8 *vs.* 5·0%, 95% CI 4·0–6·0).

DISCUSSION

In our nationwide population-based study from 1995 to 2002, we observed a significant increase in the incidence of BSI, concomitantly with an increase of the rate of blood cultures performed. An increase in the incidence was observed in most age groups and was evenly distributed between categories of microbes. The annual yield for blood cultures remained stable and there was no association between the increased incidence and a switch in individual laboratories from mail to electronic reporting, excluding enhanced reporting as the cause of the increase. The BSI incidence was highest in infants and elderly patients. Regional BSI incidence was significantly associated with regional blood-culturing activity.

We observed an average annualized BSI incidence of 125 cases/100 000 population. We believe that this is an accurate estimate, since it is based on the mandatory reporting of all Finnish clinical microbiology laboratories. There was no association between the increasing trend and a switch from mail to automated electronic notification, which also supports the conclusion that the observations are reliable for the whole period of study. Few other population-based studies on the overall BSI incidence have been published. An annual BSI incidence of 153/100 000 person-years was observed in a Danish county in 1994 [6]. In a sepsis study based on hospital discharge records in the United States in 2000, about 50% of the sepsis cases were bacteraemic, with an estimated annual BSI incidence of 122/100 000 population [4].

There was a 40% increase in the incidence of BSI during the 8-year study period, with a 5% average

Table 2. *Annual incidence of bloodstream infection (BSI) in males, Finland, 1995–2002*

Age group (years)	Annual incidence (cases per 100 000)									Change (%)*	*P* value
	1995	1996	1997	1998	1999	2000	2001	2002	1995–2002		
< 1	455	449	444	542	536	505	536	635	511	40	< 0·001
1–14	31	34	33	30	36	36	33	37	34	20	0·131
15–24	26	32	28	27	36	41	47	35	34	31	< 0·001
25–34	42	38	45	44	46	42	50	49	44	16	0·036
35–44	51	64	64	61	61	74	73	67	64	30	< 0·001
45–54	100	92	112	123	114	128	123	129	115	29	< 0·001
55–64	180	179	206	220	225	232	226	224	213	24	< 0·001
65–74	367	393	401	374	426	415	435	433	406	18	< 0·001
⩾ 75	560	664	693	659	661	769	873	783	714	40	< 0·001
All	110	118	127	128	135	145	153	151	133	38	< 0·001

* Change in rate from 1995 to 2002.

Table 3. *Annual incidence of bloodstream infection (BSI) in females, Finland, 1995–2002*

Age group (years)	Annual incidence (cases per 100 000)									Change (%)*	*P* value
	1995	1996	1997	1998	1999	2000	2001	2002	1995–2002		
< 1	397	356	323	435	512	452	431	498	424	25	0·002
1–14	29	25	32	29	31	34	25	34	30	18	0·235
15–24	28	27	33	35	38	30	45	36	34	26	0·001
25–34	36	39	38	48	51	50	46	54	45	50	< 0·001
35–44	40	46	50	44	57	48	63	51	50	28	< 0·001
45–54	60	71	80	70	78	80	96	90	78	52	< 0·001
55–64	112	119	131	127	146	138	155	159	137	42	< 0·001
65–74	234	226	248	236	242	274	285	289	254	24	< 0·001
⩾ 75	390	435	431	431	454	493	534	546	467	40	< 0·001
All	97	103	109	108	119	123	135	137	117	42	< 0·001

* Change in rate from 1995 to 2002.

annual increase, while criteria for notification remained unchanged. In England and Wales, the number of blood isolates reported increased by 61% during 1990–1998 [1] whereas in the United States where for half of the cases specific organisms causing sepsis were reported, the average annualized increase in the incidence of BSI was ~9% over a 22-year period [4].

Infants and elderly persons had the highest rates of BSI in our study, as observed in previous reports [1, 7]. Over one-quarter of our BSI cases were aged ⩾75 years. Males had higher BSI rates than females, especially among the middle-aged and elderly (RR ~1·5). In the United States, sepsis was also more common (relative risk 1·28) among men [4]. In 2003, 17% of the population was aged ⩾65 years, by 2020 the proportion is predicted to be 23% (Statistics Finland). This will have a significant impact on the burden of BSI.

In the 1980s, the increasing incidences of sepsis and BSI were associated with a growing proportion of sepsis caused by Gram-positive bacteria [4, 8]. In the British study from the 1990s, no similar association was found [1]. In our study since the mid-1990s, we did not observe any significant changes in the relative proportions of the most common blood-culture isolates. In the British study, an upward trend of possible skin contaminants, such as *Corynebacterium* spp. and diphtheroids, was reported [1] and only half of positive blood cultures were estimated to represent true BSI in a study from the United States [2]. In contrast, we found a lower proportion of possible skin contaminants, and there was no change in the annual proportion (13–15%) of these bacterial species

Table 4. *Incidence of bloodstream infection (BSI) and blood-culture sampling rate by health districts, Finland, 1995–2002*

District code	Average catchment population	Proportion of population aged ⩾65 yr	BSI†	Blood culture rate‡	BSI cases per 1000 blood cultures
1*	254 445	16	187	4900	38
2	67 872	19	158	3951	40
3*	444 768	16	149	3318	45
4	125 550	14	149	3453	43
5	78 694	15	136	3543	38
6	130 251	17	133	3713	36
7	87 276	16	133	3857	34
8*	1 363 510	12	132	3409	39
9	232 986	17	123	3446	36
10	107 607	18	123	3233	38
11	165 208	17	122	2594	47
12	175 188	17	116	3014	38
13	263 260	15	111	2712	41
14	69 559	15	109	2942	37
15*	474 815	16	109	2765	39
16	166 483	17	101	2316	44
17*	366 843	13	99	3495	28
18	207 160	16	99	2416	41
19	184 658	17	97	2053	47
20	197 588	17	90	2188	41

* Health district with a university hospital.
† Average annual incidence (cases per 100 000 population).
‡ Cultures per 100 000 population.

(coagulase-negative staphylococci, *Micrococcus* spp., *Propionibacterium* spp., *Corynebacterium* spp., *Bacillus* spp.).

Both the blood-culture sampling rate and the BSI incidence increased during the study period, but the rate of BSI cases/1000 blood cultures performed remained stable. To our knowledge, there are no previous nationwide population-based studies comparing the annual blood-culturing activity with the overall BSI incidence. Before 1990, increasing annual blood-culturing activity was reported and associated with trends of some individual pathogens [9, 10].

In the only previous study on the effect of switching from mail to electronic laboratory reporting from Hawaii, the switch more than doubled the number of laboratory-based reports of notifiable communicable diseases [5]. In contrast, we did not observe an increase in BSI incidence with transition from mail to electronic notification. However, electronic reporting has the potential of being timely, less laborious and reducing errors. Enhanced reporting or less rigorous indications for blood-culture sampling were unlikely explanations for our increasing BSI incidence, since the annual yield per 1000 blood cultures was stable.

We observed a marked regional variation in BSI incidence, which correlated with the regional blood-culture sampling rate. The BSI incidence was also higher in health-care districts with tertiary-care university hospitals. In a previous study, the incidence of BSI was higher in a university hospital than in a community hospital, moreover, the spectrum of the blood-culture isolates was different [11].

Limitations of our study include the lack of age- and sex-specific information on blood-culture sampling, as the yield could vary by age and gender, as observed in a previous study from the United Kingdom [7]. We were unable to evaluate the contribution of comorbidities on the observed trend, since our laboratory-based surveillance data did not include information of predisposing conditions. In previous studies, most frequent predisposing factors for BSI and sepsis have been intravenous and bladder catheters, surgery, underlying diseases and immunocompromised states [2–4, 8]. Within our material, we did not have the data to describe separately the distribution and trends of nosocomial and community-acquired BSI, each of which constitute approximately half of all cases, as previously reported [2, 12]. Our data did not allow us to analyse separately polymicrobial episodes, which have been reported to constitute ~10% of all BSI episodes [2]. While analysis of BSI caused by single pathogens in the same dataset [13, 14] will allow more detailed understanding of their epidemiology and potential for prevention, where relevant, the analysis of BSI caused by all microbes offers a view of the total disease burden in the population of this serious form of infectious disease.

In conclusion, we observed an increase in the incidence of BSI, which was not explained by an increase in any particular pathogen nor by increasing reporting of possible skin contaminants or by improved reporting by the laboratories. The increasing incidence was at least partly explained by increasing blood-culturing activity, and differences in regional BSI incidences were associated with varying blood-culture sampling rates. Our findings stress the need to carry out population-based studies on the epidemiology of predisposing conditions in the ageing population for both community- and hospital-acquired BSI, as well as on diagnostic practices influencing the emerging disease burden.

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DECLARATION OF INTEREST

None.

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