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Does the incidence of infectious endocarditis show seasonal patterns? — a single center retrospective study

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Abstract: Introduction: Seasonal variation has been observed for bacterial and viral infections (e.g., COVID-19 [1]), but also for numerous cardiac problems. However, little information is available on the seasonality of infectious endocarditis (IE), a rare disease that is usually linked to a bacterial origin. Data from the Polish population are lacking.
Materials and Methods: Our retrospective study focused on the identification of patients with IE, who were hospitalized at the University Hospital in Krakow between 2005–2022. For this purpose, we searched the medical records system using the ICD-10 code. We decided to divide our patients into four groups (winter, spring, summer, autumn), based on the date of admission to the hospital. Comparison of the distribution of IE incidents by season was performed with the ch2 test.
Results: One hundred and ten patients were included in the study (median age 62.5 years (range 20–94), 72 men (65.45%)). The left native valve IE was diagnosed in 49% of the patients, the prosthetic valve IE in 16%, the right valve IE in 27% and the implantable cardiac electronic devices IE in 12% of the subjects. The outcomes comprised of cardiac surgery (n = 53), embolism (n = 16), death (n = 15) and metastatic infections (n = 5). No differences in the incidence of IE by season were observed.
Conclusions: In the preliminary observation of IE cases of patients admitted to the University Hospital in Krakow, Poland no seasonal pattern of IE was detected. Therefore, IE should be taken into account in the differential diagnosis at any time of the year.

Keywords: infectious endocarditis, IE, seasonality, heart valves, S. aureus.

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Introduction

Seasonal variation has been observed not only for various bacterial and viral infections (e.g., COVID-19 [1]), but also numerous cardiac problems (e.g., myocardial infarction occurrence rates [2]). However, little information is available on the seasonality of infectious endocarditis (IE), a rare disease usually linked with a bacterial origin. Currently, most of our knowledge on IE epidemiology comes from studies done in the American, Danish, Finnish, and Taiwanese populations. Data from the Polish population is lacking. Our study was undertaken to compare the incidence of IE in different seasons and to determine if IE caused by S. aureus is associated with a seasonal pattern.

Materials and Methods

Study design

The retrospective study was based on the identification of patients with IE, hospitalized at the University Hospital in Krakow between January 2005 to August 2022, by searching the ICD-10 code (I33, I38, and I39) in the medical records system. Modified Duke criteria scoring was used to define cases of endocarditis. The 'seasons' were defined by calendar seasons, distributing patients into 4 groups (winter, spring, summer, autumn). The date of hospital admission was used to assign the patient to the seasonal group. The study was approved by the Bioethics Committee of the Jagiellonian University (protocol number — KBET, 1072.6120.308.2021).

Statistical analysis

Statistical analyses were performed using Statistica v. 13.0 software package (StatSoft Inc., Statistica, Tulsa, OK, USA). The Kruskal–Wallis test by ranks was used to analyze quantitative variables in four subgroups. We provided median [lower quartile — upper quartile] for non-normally distributed variables. Clinical, demographic characteristics and the distribution of IE incidents by season were compared using the Chi-squared test for categorical variables. A p-value <0.05 was considered to be the threshold for statistical significance.

Results

The clinical and demographic characteristics of the study population in our hospital are shown in Table 1. The median age was 62.5 years (range 20–94) with a total of 72 men and 38 women. The most common localization of vegetation was the left native

Table 1. Characteristics of patients with IE hospitalized at the University Hospital in Krakow between January 2005 to August 2022.

Variable	All	Spring	Summer	Autumn	Winter	p-value
N (%)	110 (100.00)	34 (30.91)	29 (26.36)	24 (21.82)	23 (20.91)	0.71
Sex						
Women	38 (34.55)	12 (35.29)	10 (34.48)	13 (54.17)	3 (13.04)	0.24
Men	72 (65.45)	22 (64.71)	18 (62.07)	11 (45.83)	20 (86.96)	0.53
Median age, years	62.50 [48.00–72.00]	64.50 [50.00–78.00]	66.00 [55.00–69.00]	54.50 [41.50–69.00]	61.00 [43.00–70.00]	0.34[a]
Median BMI, kg/m^2	26.27 [22.78–32.05]	27.50 [23.29–35.60]	27.47 [24.65–35.60]	24.09 [20.72–28.08]	24.28 [23.20–29.63]	0.10[a]
IE Risk factor, N (%)						
Hypertension	64 (58.18)	16 (47.06)	22 (75.86)	12 (50.00)	14 (60.87)	0.65
Heart failure	51 (46.36)	18 (52.94)	14 (48.28)	5 (20.83)	14 (60.87)	0.22
Arrhythmia	43 (39.09)	15 (44.12)	12 (41.38)	5 (20.83)	11 (47.83)	0.41
Diabetes type 2	34 (30.91)	10 (29.41)	12 (41.38)	5 (20.83)	7 (30.43)	0.35
Coronary disease	29 (26.36)	8 (23.53)	12 (41.38)	3 (12.50)	6 (26.09)	0.38
Renal failure	28 (25.45)	10 (29.41)	7 (24.14)	6 (25.00)	5 (21.74)	0.82
Obesity	26 (23.64)	8 (23.53)	9 (31.03)	4 (16.67)	5 (21.74)	0.72
Valvular heart disease	23 (20.91)	9 (26.47)	7 (24.14)	4 (16.67)	3 (13.04)	0.57
Foreign bodies	22 (20.00)	4 (11.76)	10 (34.48)	3 (12.50)	5 (21.74)	0.51
Artificial valve-biological	15 (13.64)	6 (17.65)	2 (6.90)	2 (8.33)	5 (21.74)	0.62
Artificial valve-mechanical	10 (9.09)	2 (5.88)	3 (10.34)	2 (8.33)	3 (13.04)	0.98
Reduced immunity	18 (16.36)	4 (11.76)	4 (13.79)	7 (29.17)	3 (13.04)	0.82
Congenital heart disease	6 (5.45)	1 (2.94)	1 (3.45)	3 (12.50)	1 (4.35)	0.85
IV drugs abuse	5 (4.55)	1 (2.94)	2 (6.90)	0 (0.00)	2 (8.70)	0.65
Rheumatic heart disease	1 (0.91)	0 (0.00)	1 (3.45)	0 (0.00)	0 (0.00)	0.75
Localization of IE, N (%)						
Left IE natural valve	54 (49.09)	19 (55.88)	16 (55.17)	13 (54.17)	6 (26.09)	0.26
Left IE artificial valve	18 (16.36)	5 (14.71)	4 (13.79)	3 (12.50)	6 (26.09)	0.90
Right IE	30 (27.27)	8 (23.53)	7 (24.14)	5 (20.83)	10 (43.48)	0.83
Connection with diverse	13 (11.82)	3 (8.82)	5 (17.24)	0 (0.00)	5 (21.74)	0.26
Multiple	5 (4.55)	2 (5.88)	1 (3.44)	1 (4.17)	1 (4.35)	0.97
Blood culture positive rate, N (%)	78 (70.91)	22 (64.71)	23 (79.31)	19 (79.17)	14 (60.87)	0.71
Organisms, N (%)						
S. aureus	38 (34.55)	11 (32.35)	12 (41.38)	6 (25.00)	9 (39.13)	0.75
S. species	14 (12.73)	3 (8.82)	4 (13.79)	5 (20.83)	2 (8.70)	0.86
Enterococcus	12 (10.91)	4 (11.76)	4 (13.79)	4 (16.67)	0 (0.00)	0.33

Table 1. cont.

Variable	All	Spring	Summer	Autumn	Winter	p-value
S. epidermidis	3 (2.73)	0 (0.00)	2 (6.90)	0 (0.00)	1 (4.35)	0.55
Candida	2 (1.82)	0 (0.00)	0 (0.00)	2 (8.33)	0 (0.00)	0.49
HACEK	0 (0.00)	0 (0.00)	0 (0.00)	0 (0.00)	0 (0.00)	–
Others	13 (11.82)	3 (8.82)	3 (10.34)	5 (20.83)	2 (8.70)	0.88
Complication of IE, N (%)						
Cardiosurgery	53 (48.18)	17 (50.00)	16 (55.17)	6 (25.00)	14 (60.87)	0.32
Urgent cardiac surgery	42 (38.18)	13 (38.24)	13 (44.83)	6 (25.00)	10 (43.48)	0.62
Failure the valve	51 (46.36)	16 (47.06)	13 (44.83)	10 (41.67)	12 (52.17)	0.87
Embolization	16 (14.55)	4 (11.76)	4 (13.79)	5 (20.83)	3 (13.04)	0.97
Death	15 (13.64)	5 (14.71)	2 (6.90)	2 (8.33)	6 (26.09)	0.62
Metastatic infection	5 (4.55)	2 (5.88)	1 (3.45)	2 (8.33)	0 (0.00)	0.35

P-value for the ch2 test; p-value[a] for the Kruskal-Wallis test by ranks.
BMI — body mass index; IE — infective endocarditis; HACEK — Haemophilus species, Aggregatibacter, Cardiobacterium, Eikenella, Kingella.

valve which accounted for 49% of all cases, followed by the right valve (27%), prosthetic valve (16%), multiple valves (5%) and connection with cardiac implantable electronics devices (12%). Among our patients, 58% had hypertension, 46% had prior heart failure, 39% had arrhythmia and 31% had diabetes type 2. The outcomes included cardiac surgery (48%), the valvular dysfunction (46%), embolism (15%) and death (14%). There were no differences in the incidence and outcome of IE based on seasonal incidence: winter 20.91%, spring 30.91%, summer 26.36%, and autumn 21.82%; p = 0.71. Infections caused by S. aureus (n = 38) also did not present in a seasonal pattern; p = 0.75.

Discussion

Knowledge of seasonal trends in rare clinical conditions like infective endocarditis may improve surveillance especially in high-risk groups and help guide the strategies of infection prevention interventions. There are many different conditions, including bacterial infections, showing seasonal patterns. The causes of these observation may be related with biology of the pathogens but also with the human physiological and life style changes under seasonal variations. Recently, it was documented that endogenous seasonal variability in human immune response exists, which is independent of a wide range of demographic and environmental factors [3]. Moreover, large eight-year study of 132 hospitals in the United Stated showed significant increases in the frequency of inpatient bloodstream infection in summer [4]. Taking into account above, we have undertaken the study to analyze the seasonality of the incidence and clinical outcome

of infective endocarditis. In our single center study we did not find significant association between seasons and the incidence of infective endocarditis neither its outcome and etiology.

In contrary, a fall/winter surge in IE has been shown in a single study including 269 cases performed in the USA [5]. However, no clinical factors were identified that could explain this finding. On the other hand, the results of studies conducted on the Danish [6] and Finnish [7] population are not in line with American findings. It is important to mention that Athela *et al.* have demonstrated that patients admitted to hospitals in Finland due to IE in the summer had a higher 1-year mortality compared to patients admitted in winter [7].

An interesting observation was reported by scientists from Taiwan. Chen *et al.* identified the presence of left ventricular systolic dysfunction, left ventricular hypertrophy, Staphylococcal infection, and the low temperatures of IE episodes as independent poor outcome predictors for all-cause hospital mortalities in patients with IE. Moreover, scientists demonstrated that the mortality rate in the fall/winter was 2.6-fold higher than that in the spring/summer groupings [8]. In addition, Desimone *et al.* proved an increase in IE incidence caused by Staphylococcus aureus in the winter season [5]. In our study in-hospital mortality was the highest in winter and the lowest in summer and autumn, but this differences did not reach statistical significance. There are several limitations of our study. The most important may be selection bias as only patients enrolled in one hospital were enrolled in this investigation and the number of patients included is relatively small. Accordingly, we plan to perform further analysis in a larger group of patients admitted to multiple hospitals throughout Poland. Additional bias may be related to the assignment of patients to the seasonal groups, as the symptoms may have started much earlier in time potentially leading to the misclassification of the patient. Nevertheless, the time interval between IE first symptoms and diagnosis is closely related to the IE clinical presentation, patient characteristics and causative microorganism, and therefore this delay me be considered as systematical in the population under study and the date of hospital admission remains the most reliable and reasonable for analyses performed.

Conclusions

In conclusion, in the preliminary observation of IE cases of patients admitted to the University Hospital in Krakow, Poland no seasonal pattern of IE was detected. Therefore, IE should be taken into account in the differential diagnosis at any time of the year. It is crucial to have high clinical suspicion of this diagnosis in all febrile and septic patients as a potential concomitant infection even during seasonal-dependent infectious diseases such as influenza or COVID-19.

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Conflict of interest

None declared.

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