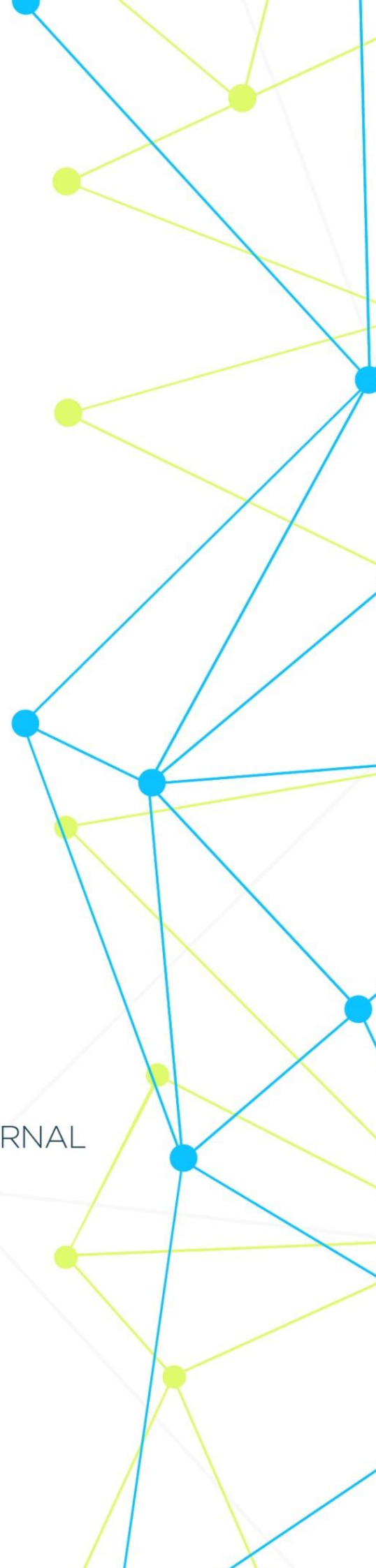


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**The importance of the criteria of systemic inflammatory Response syndrome of early
diagnostics and detection of bloodstream infections**

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Summary

Purpose of study

Determine the frequency of detection of patients with bloodstream infections (BSI) with applying systemic inflammatory response syndrome (SIRS) criteria, and analyze the clinical characteristics of patients with suspected BSI.

Methods

In the study were included 1,463 patients hospitalized in various departments according to their primary diagnosis. Indication for study inclusion and hemoculture collection of patients was the detection of at least 2 or more criteria of SIRS (ACCP/SCCM, Atlanta, 1992), in accordance with the protocol of the POP project "Proof-of-principle routine diagnostic project for a Antimicrobial Resistance Surveillance", with technical support from WHO, during the period from 2019-2020.

The obtained results

The largest number of patients (376) was admitted to the intensive care unit, 293 patients each admitted to the pediatric and infectious disease units and 183 patients admitted to the diagnostic units. All characteristic clinical symptoms of SIRS occurred in the examined patients. Hyperthermia was the most common in all age groups - in 47 patients in 74.60±1.08% of cases in the group of patients under one year of age, significantly more frequent in the group of 1-5 years (594), 5-12 years (166), 12-18 and over 18 years (60; 486, respectively $P < 0.05$). Tachycardia was also frequently observed in all age groups - almost in all patients (91.9±0.99%) in the group less than 1 year old, almost equally often in 75±0.66% and 73.90±0.38% of cases in the group 5-12 and over 18 years old, respectively. This symptom was noted in more than 50% of cases in patients in the 1-5 (65%) and 12-18 (84%) age group. Tachypnea and leukocytosis were most frequently observed in patients under 1 year of age (47.62±0.87% and 71.43±1.06%, respectively), whereas in the remaining groups (1-5, 5-12, 12-18, and over 18 years of age), leukocytosis was noted in 63%, 50%, 59%, and 58% of cases, respectively, and tachypnea in 23%, 10%, 19%, and 25%, respectively. A combination of 2 symptoms (hyperthermia and tachycardia), a combination of hyperthermia and leukocytosis in 18.1% of cases, a triad of symptoms tachycardia, hyperthermia and leukocytosis in 23.9% of cases was the most common (41.5%) of the criteria for SSRI. Also often enough (6.8%) were observed 4 symptoms hyperthermia, tachycardia, tachypnoea and leukocytosis.

Conclusions

The most frequent localization of infection in BSI was the upper respiratory tract, lower respiratory tract infections were detected twice as often. Predominantly, regardless of the

localization of infection, a combination of the criteria for SIRS of two symptoms was observed. Irrespective of the localization of infection, all patients had fever in various combinations, most frequently with tachycardia (26.8%) and leukocytosis (26.2%).

Keywords Bloodstream infections, systemic inflammatory response syndrome, sepsis, hyperthermia, tachycardia, tachypnea, leukocytosis, neutrophilia.

Introduction

Bloodstream infections (BSIs) are defined as the presence of bacteria in the blood detected by hemoculture testing. This definition includes all clinical manifestations of BSI, including systemic inflammatory response syndrome (SIRS/SIRS, the initial manifestation of BSI), sepsis (life-threatening illness accompanied by organ dysfunction due to dysregulated host response to infection) and septic shock (sepsis accompanied by persistent pressure drop despite rehydration, plus impaired cellular metabolism) [1]. Bloodstream infections are among the most common diagnoses treated in intensive care units. According to some author reports, 1.7 million patients develop BSIs each year in the United States, most of whom are over 65 years of age [2]. Mortality, which reaches 10% in patients with sepsis and 40% in patients with septic shock, is usually the result of multiple organ dysfunction syndrome (MODS) [3].

The introduction of the use of the SIRS criteria proposed at the consensus conference of the American College of Thoracic Surgeons and Society of Emergency Physicians would be an indication for hemoculture testing and would allow identification of patients at risk for sepsis and MODS, and would facilitate early intervention and appropriate management tactics .

SIRSSs are characterized by a wide range of conditions and may have a severe clinical course. The main clinical and laboratory indicators for the diagnosis of SIRS are body temperature above 38.3°C (fever) or below 36°C (hypothermia), heart rate more than 90 beats per minute (tachycardia), respiratory rate more than 20 breaths per minute (tachypnea), white blood cell count more than $12 \times 10^9/L$ or less than $4 \times 10^9/L$ or more than 10% immature neutrophils (stabial forms). SIRS criteria for children are presented in Table 1 according to the age of the child.

Table 1. Specific age criteria for SIRS

Age group	body temperature (°C)		heart rate (beats per minute)		respiratory rate (breaths per minute)	white blood cell count (in $10^9/L$)
	fever	hypothermia	tachycardia	bradycardia		
Newborn (0 days to 1 week)	>38,3	<36,0	>180	<100	>50	>34
Newborn (1 week to 1 month)	>38,3	<36,0	>180	<100	>40	>19,5 or <5

Infant (1 month to 1 year)	>38,3	<36,0	>180	<90	>34	>17,5 or <5
Pre-school age (from 1 to 5 years)	>38,3	<36,0	>140	HPI	>22	>15,5 or <6
School age (5 to 12 years old)	>38,3	<36,0	>130	HPI	>18	>13,5 or <4,5
Teenagers (12 to 18 years old)	>38,3	<36,0	>110	HPI	>14	>11 or <4,5

The presence of two or more of the above signs against the background of infection and bacteremia is interpreted as a systemic inflammatory response to the infection, i.e., SIRS [4,5,6].

The purpose of our study is to determine the frequency of detection of patients with bloodstream infections when applying the criteria of systemic inflammatory response syndrome, and to analyze the clinical characteristics of patients with suspected bloodstream infections.

Materials and Methods

In the study were included 1,463 patients hospitalized in various departments according to their primary diagnosis. Indication for study inclusion and hemoculture collection of patients was the detection of at least 2 or more criteria of SIRS (ACCP/SCCM, Atlanta, 1992), in accordance with the protocol of the POP project "Proof-of-principle routine diagnostic project for a Antimicrobial Resistance Surveillance", with technical support from WHO, during the period from 2019-2020.

From the total number of patients, 42% were female (615) and 58% male (848). The age of the patients ranged from a few months to 90 years (up to 1 year - 5%, 1-5 years - 45%, 5-12 years - 12%, 12-18 years - 4%, and over 18 years - 34%).

In the selected patients we analyzed medical history data, clinical parameters in accordance with SIRS criteria, the fact of taking antibiotics at the time of blood sampling, empirical therapy before the bacteriological test result of hemoculture, and the tactics of antibiotic therapy after a positive result from the bacteriological laboratory.

Obtained results

All patients were hospitalized in different departments of huge multidisciplinary hospitals of Tashkent, Uzbekistan (Table 2).

Table 2. Distribution of patients according to departments

Departments	n	%
1. Adults ICU	376	25,7±0,13
2. Pediatric/Newborn	296	20,23±0,12
3. Infectious Diseases	293	20,03±0,12
4. Diagnostic	183	12,51±0,09

5. Pediatric/Newborn ICU	95	6,49±0,07
6. Therapeutic	92	6,29±0,07
7. Surgical	91	6,22±0,07
8. Urologic	34	2,32±0,07
9. Rehabilitation	3	0,21±0,04

Comparative analysis of the obtained data showed that the largest number of patients (376) were hospitalized in the intensive care unit ($p < 0.05$). Between the number of patients hospitalized in pediatric (293), infectious diseases (293) and diagnostic (183) departments significance was not noted. Hospitalization of the examined patients in the neonatal intensive care unit, therapeutic and surgical departments was equally frequent ($p > 0.05$). Hospitalization of patients at the urologic department and rehabilitation department was significantly less frequent, and showed only in $2.32 \pm 0.07\%$, $0.21 \pm 0.04\%$ cases, respectively ($p < 0.05$).

The distribution of patients according to SIRS clinical criteria at the time of hospitalization is shown in Table 3.

Table 3. Clinical parameters of the whole group of patients according to age

Clinical parameters	Under 1 year old	1 - 5 years old	6-12 years old	13 – 18 years old	Older than 18 years old
hyperthermia	74,60±1,08	90,69±0,37*	96,51±0,75*°	80,00±1,03*°^	97,597±0,44*°•
hypothermia	3,17±0,22	2,9±0,07	3,49±0,14°	-	1,20±0,05*°^•
tachycardia	91,9±0,99	50,84±0,28*	75±0,66*°	61,33±0,90°^	73,90±0,38*°•
bradycardia	-	0,46±0,03*	0,58±0,06*	-	1,41±1,08*°^•
tachypnea	47,62±0,87	20,15±0,18*	8,72±0,23*°	16,00±0,46*°^	21,08±0,21*°^•
leukocytosis	71,43±1,06	59,69±0,30*	46,51±0,52*°	49,33±0,81*°^	55,02±0,33*°^•
leukopenia	4,76±0,27	1,37±0,05*	1,74±0,10*°	1,33±0,13*	1,20±0,05*
neutrophilia	3,17±0,22	0,76±0,03*	1,16±0,08*°	-	0,80±0,04*°^•

Note: * Comparison of indicators with the group of patients under 1 year of age ($p < 0.05$)

° Comparison of indicators with the group of 1-5 years, ($p < 0.05$)

^ Comparison of indicators with the group of 5-12 years, ($p < 0.05$)

- Comparison of indicators with the group of 12-18 years, ($p < 0.05$)

The examined patients had all clinical symptoms of SIRS. The most common in all age groups was hyperthermia: in the 1-5 years group and in over 18 year's group it amounted significantly more frequent 594 ($p < 0.05$) and 486 of cases ($p < 0.05$), respectively. In the 6-12 years group – in 166 of cases, in the 13-18 – in 60 of cases, and in the group of patients under one year of age it amounted 47 patients ($74.60 \pm 1.08\%$ of cases), which shows that it was not had significant difference. Tachycardia were also frequently observed in all age groups - nearly all patients ($91.9 \pm 0.99\%$, $p < 0.05$) in the group less than 1 year old, almost equally often in $75 \pm 0.66\%$ and

73.90±0.38% of cases in the group 5-12 and over 18 years old, respectively. In more than 50% of cases this symptom was observed in patients in the age group of 1-5 (65%) and 12-18 (84%) years old. Such symptoms as tachypnoea and leukocytosis were most frequently observed in patients under 1 year of age (47.62±0.87% and 71.43±1.06%, respectively), whereas in the remaining groups (1-5, 5-12, 12-18 and over 18 years old), leukocytosis was noted in 63%, 50%, 59% and 58%, respectively, and tachypnoea in 23%, 10%, 19% and 25%, respectively.

We divided all the examined patients into groups according to combinations of symptom occurrence. The results showed that the most common combination of 2 characteristic clinical symptoms was registered in 758 patients (51.8%), in 590 patients (40.3%) of 3 symptoms, and in 115 cases (7.9%) 4 symptoms were encountered. But there was no statistical reliability in the distribution of patients into groups. ($p>0.05$).

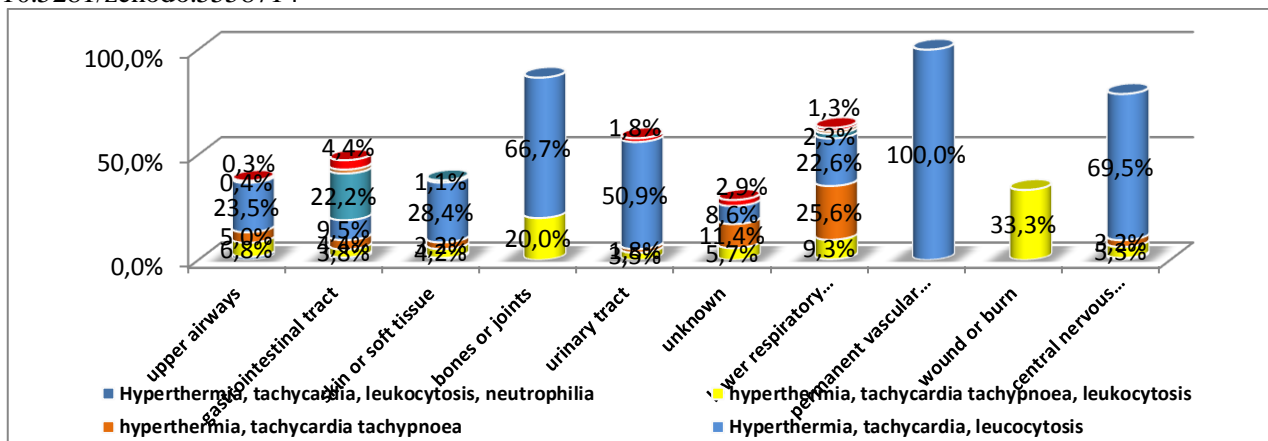
Table 4. Distribution of patients into groups according to combinations of SIRS criteria

Groups	Combinations of SIRS criteria	Quantity (n, %)
1 group	2 symptoms	758 (51,8%)
2 group	3 symptoms	590 (40,3%)
3 group	4 symptoms	115 (7,9%)

Table 5. Combination of SIRS criteria

Combination of SIRS criteria	Quantity (%)	Quantity (n)
Hyperthermia + tachycardia	26,8%	392
hyperthermia + tachycardia + leucocytosis	26,2%	384
hyperthermia+leukocytosis	20,6%	301
hyperthermia+tachycardia+tachypnoea	9,0%	132
hyperthermia+tachycardia+tachypnoea+leukocytosis	6,7%	98
tachycardia+tachypnoea+leukocytosis	3,3%	48
hyperthermia+tachycardia+leukocytosis+neutrophilia	1,0%	15
hyperthermia+tachypnoea	1,0%	15
tachycardia+tachypnea	0,6%	9
leukocytosis+tachypnea	0,5%	8
tachycardia+tachypnoea+hypothermia	0,5%	7

Combinations of SIRS criteria depending on the presumed localization of infection are shown in Fig.1a, and Fig.1b



Analysis of the occurrence of various combinations of SIRS criteria in the surveyed group of patients showed that the most frequent was a combination of two symptoms: in 62.2% for localization on the skin and soft tissues, in 61.7% in the upper respiratory tract, and in 52.5% for a source of infection in the gastrointestinal tract. The greatest combination of three SSRI criteria was observed in the lower respiratory tract (53.1%) and gastrointestinal tract (42.4%).

Combinations of SSRS criteria of hyperthermia, tachycardia and tachypnoea were observed in 26.6% of cases with localization of infection in the lower respiratory tract (301), 22.6% of hyperthermia, tachycardia and leucocytosis, 9.6% of hyperthermia, tachypnoea and leucocytosis, in 20.3% of cases there was a combination of 2 symptoms - hyperthermia and leucocytosis, and in 14.3% of hyperthermia and tachycardia.

Figure 1a - Combinations of SIRS

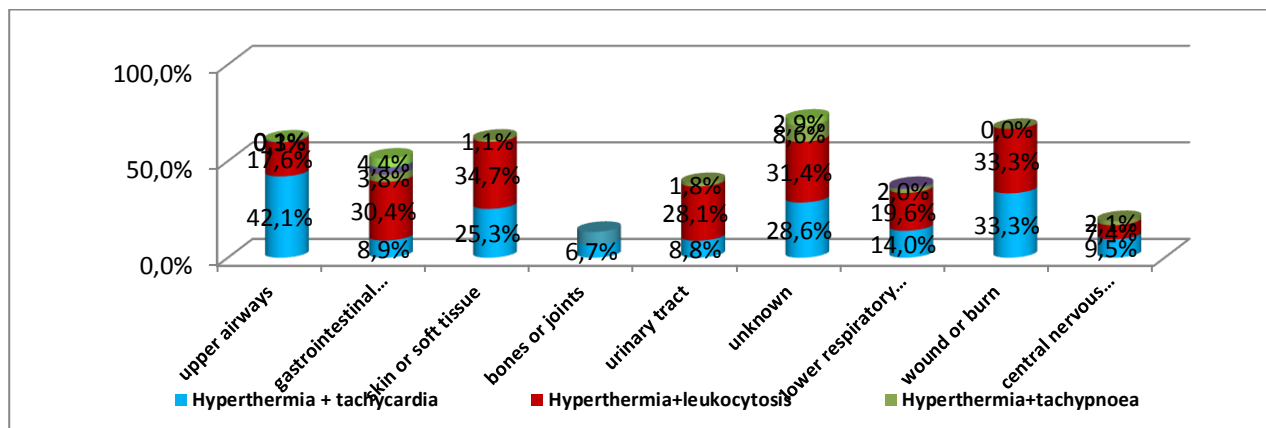


Figure 1b - Combinations of SIRS

When we analyzed the localization of infection in our patients with suspected BSI, the most frequent was in the upper respiratory tract (703), accounting for 48.1%; in the lower respiratory tract - 301 patients, accounting for 20.6%. Gastrointestinal diseases accounted for 10.8% (158) of the cases ($p \geq 0,05$) Fig.2a, 2b, 2c.

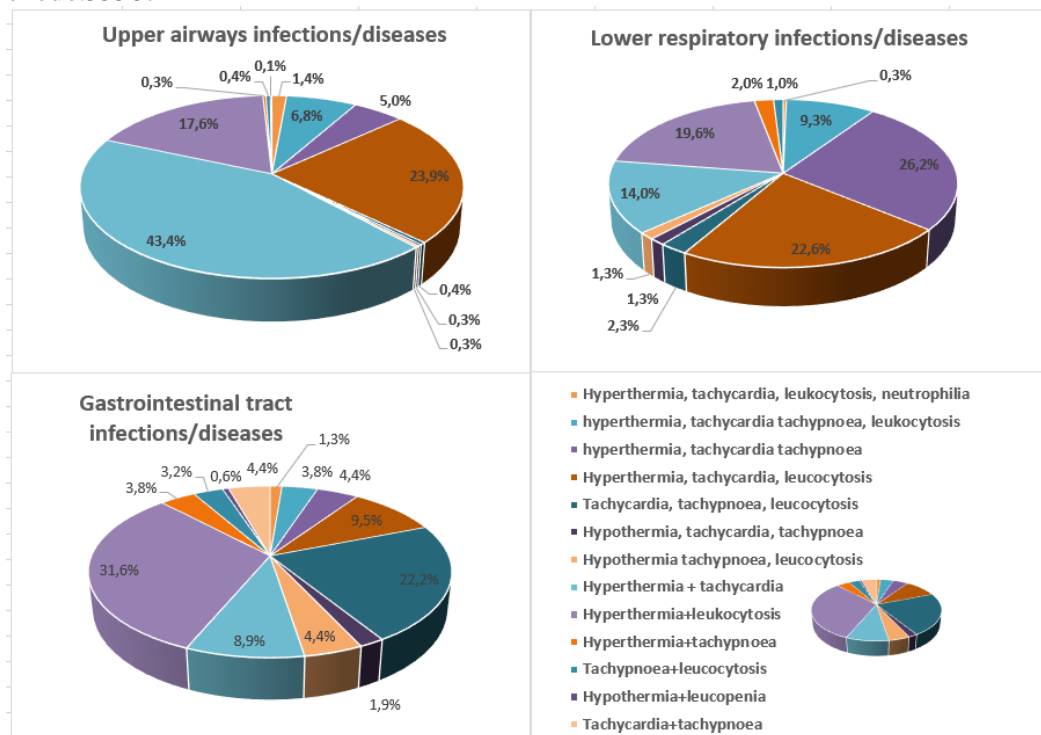


Fig. 2a, 2b, 2c Combinations of SIRS criteria depending on the presumed localization of infection

In this group of patients, a combination of 2 symptoms (hyperthermia and tachycardia), in 18.1% of cases a combination of hyperthermia and leukocytosis, and in 23.9% of cases a triad of symptoms - tachycardia, hyperthermia and leukocytosis - was observed most frequently. The 4 symptoms of hyperthermia, tachycardia, tachypnoea and leucocytosis were also common (6.8%).

In the gastrointestinal tract, a combination of hyperthermia and leucocytosis (30.4%) was more frequent, hyperthermia, tachycardia with leucocytosis was shown in 9.5% of cases, and less frequent were the criteria of SIRS such as hyperthermia with tachycardia, in 8.9% ($p \leq 0.05$).

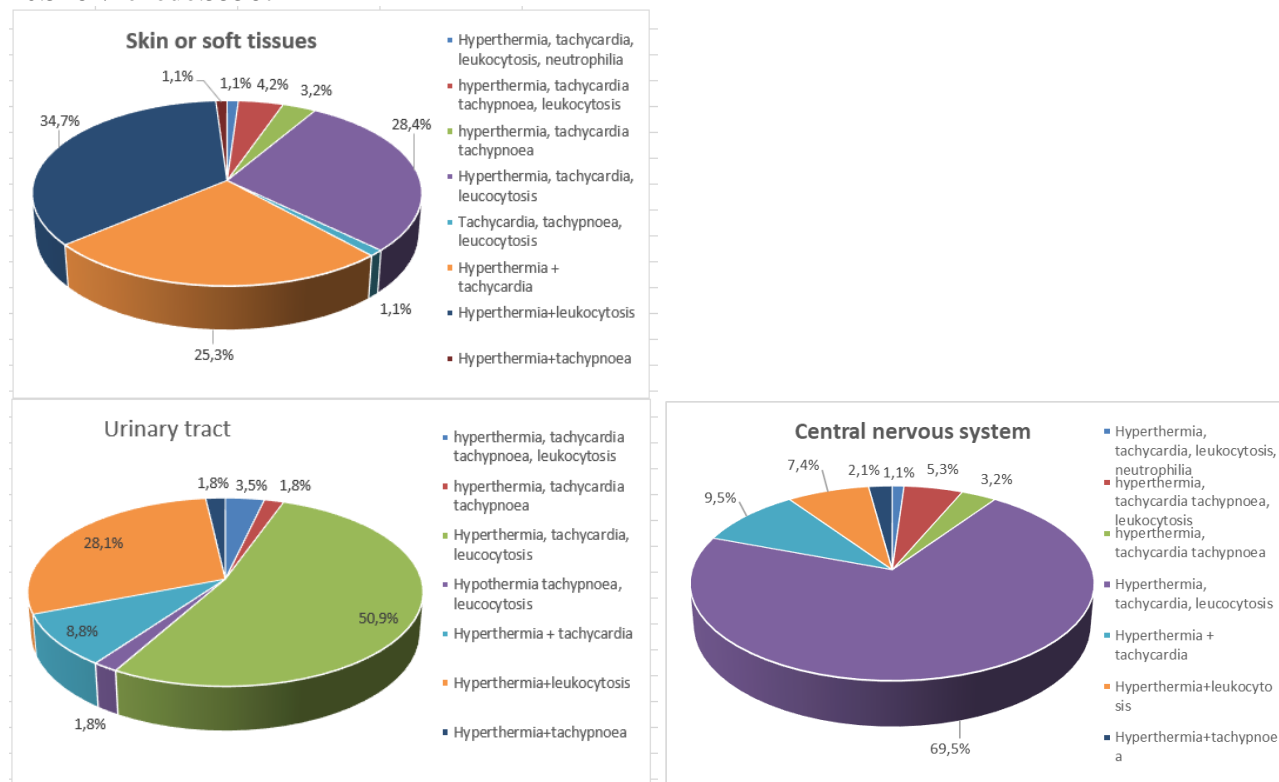


Fig.3a, 3b, 3c. Combinations of SIRS criteria depending on the presumed localization of infection

More than half of the cases (51.8%) showed a combination of three symptoms: hyperthermia, tachycardia and leucocytosis, and 28.6% showed a combination of 2 symptoms: hyperthermia and leucocytosis, if the infection was localized in the urogenital tract (Fig. 3b).

A comparative analysis of the results showed that irrespective of the localisation of infection, all patients had fever in various combinations, most frequently with tachycardia (26.8%) and leucocytosis (26.2%).

Thus, all the characteristic clinical symptoms of SIRS were mostly present. Hyperthermia was the most common in all age groups. The most frequent localization of infection in BSI was in the upper respiratory tract (702), accounting for 48.1%, ($p>0.05$); almost half as many were in the lower respiratory tract, 301 patients, accounting for 20.6%, ($p>0.05$). In 10.8% (158) of cases, the development of septic conditions was observed in gastrointestinal diseases. Analysis of the occurrence of various combinations of SIRS criteria in the examined group of patients showed that the most frequent was a combination of two symptoms: in 62.2% for localization in the skin and soft tissues, in 61.7% in the upper respiratory tract, and in 52.5% for a source of infection in the gastrointestinal tract ($p<0.05$). The most frequent combination of three SIRS criteria was observed in the lower respiratory tract (53.1%) and gastrointestinal tract (42.4%). A comparative analysis of the findings showed that irrespective of the localisation of infection, all patients had fever in varying combinations, most frequently with tachycardia (26.8%) and leucocytosis (26.2%), $p>0.05$.

Conclusions.

1. The upper respiratory tract, lower respiratory tract infections was the most frequent localization of infection in BSI.
2. Predominantly, irrespective of the localization of infection, a combination of the criteria for SIRSs of two symptoms was observed.
3. Irrespective of the localization of infection, all patients present with fever in varying combinations, most commonly with tachycardia (26.8%) and leucocytosis (26.2%).

Conflict of interest

The authors declare no conflict of interest.

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