



Paper Accepted*

ISSN Online 2406-0895

Original Article / Оригинални рад

Aleksandra Doronjski^{1,2}, Milena Bjelica^{1,†}, Slobodan Spasojević^{1,2},
Tanja Radovanović¹, Jelena Ćulafić¹, Vesna Stojanović^{1,2}

Sudden death in children

Изненадна смрт код деце

¹ Institute for Child and Youth Health Care of Vojvodina, Novi Sad, Serbia;

² University of Novi Sad, Faculty of Medicine, Novi Sad, Serbia

Received: January 13, 2017

Revised: May 4, 2017

Accepted: May 12, 2017

Online First: May 23, 2017

DOI: <https://doi.org/10.2298/SARH170113114D>

* **Accepted papers** are articles in press that have gone through due peer review process and have been accepted for publication by the Editorial Board of the *Serbian Archives of Medicine*. They have not yet been copy edited and/or formatted in the publication house style, and the text may be changed before the final publication.

Although accepted papers do not yet have all the accompanying bibliographic details available, they can already be cited using the year of online publication and the DOI, as follows: the author's last name and initial of the first name, article title, journal title, online first publication month and year, and the DOI; e.g.: Petrović P, Jovanović J. The title of the article. *Srp Arh Celok Lek*. Online First, February 2017.

When the final article is assigned to volumes/issues of the journal, the Article in Press version will be removed and the final version will appear in the associated published volumes/issues of the journal. The date the article was made available online first will be carried over.

† **Correspondence to:**

Milena BJELICA

Institute of Child and Youth Health Care of Vojvodina, Hajduk Veljkova 10, 21000 Novi Sad, Serbia

E-mail: milenabjelica@yahoo.com

Sudden death in children

Изненадна смрт код деце

SUMMARY

Introduction/Objective Sudden death in children may occur as a result of many diseases and accidents, while often the cause remains unknown. There are different terms in the literature that represent the causes of sudden death in children.

The aim of our study was to determine the most common cause of sudden death in children admitted to the Clinic of Pediatrics.

Methods The retrospective study was conducted in the period from 01.01.1995 to 30.12.2015. and included 49 patients, aged from 10 days to 17 years, in whom death occurred in the Emergency department and in the first 48 hours of hospitalization,

Results In 23 patients (47%) cause of death was infection, in 10 patients (20%) heart failure, 4 patients (8%) died due to status epilepticus, the same number of patients (8%) died due to aspiration of a foreign body, while the rest of them died due to diabetic ketoacidosis (2%), rickets (2%), carbon monoxide poisoning (2%), hemolytic anemia (2%), suicide by hanging (2%), drowning (2%), sudden infant death syndrome (2%) and sudden unexpected death in epilepsy (2%). Most patients in our study were infants (43%).

Conclusion Our study shows that infants are at the highest risk of sudden death, while the most frequent causes of death are infections and cardiovascular diseases.

Keywords: sudden death; child; infant

САЖЕТАК

Увод/Циљ Изненадна смрт код деце може настати као последица многих обољења и акцидената, док врло често узрок остаје непознат. У литератури се срећу различити термини који означавају узроке изненадних смрти код деце.

Циљ овог рада је био да се утврде најчешћи узроци изненадне смрти деце примљених на Клинику за педијатрију.

Метод Ретроспективном студијом за период од 01.01.1995. до 31.12.2015. обухваћено је 49 деце, узраста од 10 дана до 17 година, код којих је смртни исход наступио у Амбуланти за ургентан пријем и у првих 48 часова хоспитализације.

Резултати Код 23 деце (47%) узрок смрти је била инфекција, код 10 (20%) срчана инсуфицијенција, код 4 (8%) радило се о епилептичком статус, код 4 (8%) смрт је наступила због аспирације страног тела, а по једно дете (2%) је егзистирало услед дијабетесне кетоацидозе, рахитиса, интоксикације угљен моноксидом, хемолитичке анемије, суицида вешањем, акциденталног утапања, синдрома изненадне смрти одојчета и изненадне неочекиване смрти код епилепсије. Највећи број у нашој студији била су одојчад (43%).

Закључак Наша студија је показала да су одојчад у највећем ризику од изненадног смртног исхода, а да су најчешћи узроци изненадне смрти код деце инфекције и кардиоваскуларне болести.

Кључне речи: изненадна смрт; дете; одојче

INTRODUCTION

The death of a child represents a dreadful event for the child's parents and for the doctors who participate in treatment of a child, especially if it is unexpected. When clinicians are faced with an imminent child death they must carry out many complex tasks. They need to treat a patient experiencing an acute medical situation, establish a compassionate relationship with patient's family and support and work in team fashion with their colleagues as they acknowledge the human limitations to remedy a medical crisis [1].

About 10% of pediatric deaths after the first year of life are sudden and population based studies put the individual age related risk at around 1:20 000 to 1:50 000 per year [2].

The death certificate diagnoses in case of pediatric sudden death may not be completely accurate, particularly in cases that have not had an autopsy [3].

The death of a child can be expected and explained (e.g. a child with malignancy who dies under appropriate circumstances, from complications of the underlying disease), expected and unexplained (e.g. a child with malignancy who dies earlier than expected or under unexplained

circumstances), unexpected and explained (e.g. road traffic accident, meningococcal sepsis) and unexpected and unexplained (e.g. sudden infant death syndrome) [4]. Sudden death in children may occur as a result of infection, heart disease, malignant disease, asthma, aspiration or airway obstruction, congenital anomaly, genetic disorder, seizure, injury, suicide, homicide, etc., while often the cause remains unknown [2,4,5]. Death can occur in outpatient conditions, in emergency department or during the hospitalization of the patient [4].

There are different terms in the literature that represent the causes of sudden death (Table 1) [1, 2, 5-8].

Table 1. Terms which define causes of sudden death.

Term	Definition
Sudden unexpected death in infants and children (SUDIC)	Sudden and unexpected death of an infant or a child
Sudden unexpected infant death (SUID) or sudden unexpected death in infancy (SUDI)	Sudden and unexpected death of an infant, explained or unexplained
Sudden infant death syndrome (SIDS)	Sudden death of an infant which remains unexplained after a thorough case investigation, including performance of a complete autopsy, examination of the death scene, and review of the child's medical history
Sudden unexplained death in childhood (SUDC)	Sudden death of a child older than 1 year of age that remains unexplained after a thorough case investigation, including performance of a complete autopsy, examination of the death scene, and review of the child's medical history
Sudden unexpected death from infectious disease (SUIDID)	Sudden and unexpected death caused by infectious disease
Sudden cardiac death (SCD)	Sudden and unexpected death caused by cardiovascular disease
Sudden unexpected death in epilepsy (SUDEP)	Sudden, unexpected, witnessed or unwitnessed, non-traumatic or non-drowning death of people with epilepsy, with or without evidence of a seizure, excluding documented status epilepticus and in whom postmortem examination does not reveal a structural or toxicological cause of death

Sudden unexpected infant death (SUID), also known as sudden unexpected death in infancy (SUDI), is a term used to describe any sudden and unexpected death, whether explained or unexplained (including sudden infant death syndrome (SIDS) and ill-defined deaths) occurring during infancy. After case investigation, SUID can be attributed to suffocation, infection, ingestions, metabolic diseases, arrhythmia, trauma etc. [9]. The most frequently reported causes of SUID are sudden infant death syndrome (SIDS), ill-defined and unknown cause of mortality, and accidental sleep-related suffocation. However, it is not always easy to differentiate explained and unexplained SUID [10].

Sudden infant death syndrome (SIDS) is the most common form of SUID and the leading cause of infant death. It is defined as sudden death of an infant which remains unexplained after a thorough case investigation, including performance of a complete autopsy, examination of the death scene, and

review of the child’s medical history [11,12]. In order to more precisely define SIDS a new classification was offered (San Diego definition from 2004) according to which SIDS is divided into categories depending on the patient's medical history, examination of the circumstances of death and the findings and completeness of the autopsy (Table 2) [13]. Risk factors for SIDS are: irregular

Table 2. San Diego definition of SIDS.

	Clinical	Circumstances of death	Autopsy
SIDS general definition	<ul style="list-style-type: none"> • Sudden and unexpected death of an infant under 1 year of age. • Fatal episode occurring during sleep. • Death unexplained by clinical history. 	<ul style="list-style-type: none"> • Death unexplained after review of the circumstances. 	<ul style="list-style-type: none"> • Death unexplained after complete autopsy.
IA SIDS*	<ul style="list-style-type: none"> • More than 21 days and <9 months of age. • Normal clinical history, including term pregnancy (gestational age of ≥ 37 weeks). • Normal growth and development. • No similar deaths among siblings, close genetic relatives (uncles, aunts, or first-degree cousins), or other infants in the custody of the same caregiver. 	<ul style="list-style-type: none"> • Investigation of the various scenes where incidents leading to death might have occurred and determination that they do not provide an explanation for the death. • Found in a safe sleeping environment, with no evidence of accidental death. 	<ul style="list-style-type: none"> • Absence of potentially fatal pathologic findings. Minor respiratory system inflammatory infiltrates are acceptable; intrathoracic petechial hemorrhage is a supportive but not obligatory or diagnostic finding. • No evidence of unexplained trauma, abuse, neglect, or unintentional injury. • No evidence of substantial thymic stress effect (thymic weight of <15 g and/or moderate/severe cortical lymphocyte depletion). Occasional “starry sky” macrophages or minor cortical depletion is acceptable. • Negative results of toxicologic, microbiologic, radiologic, vitreous chemistry, and metabolic screening studies.
IB SIDS†	<ul style="list-style-type: none"> • The same as for IA SIDS. 	<ul style="list-style-type: none"> • Investigation of the various scenes where incidents leading to death might have occurred was not performed. 	<ul style="list-style-type: none"> • One of the following analyses was not performed: toxicologic, microbiologic, radiologic, vitreous chemistry, or metabolic screening studies.
II SIDS‡	<ul style="list-style-type: none"> • Age range outside that of category IA or IB (ie, 0–21 days or 270 days [9 months] through first birthday). • Similar deaths among siblings, close relatives, or other infants in the custody of the same caregiver that are not considered suspect for infanticide or recognized genetic disorders. • Neonatal or perinatal conditions (for example, those resulting from preterm birth) that have resolved by the time of death. 	<ul style="list-style-type: none"> • Mechanical asphyxia or suffocation caused by overlaying not determined with certainty. 	<ul style="list-style-type: none"> • Abnormal growth and development not thought to have contributed to death. • Marked inflammatory changes or abnormalities not sufficient to be unequivocal causes of death.
Unclassified sudden infant death	<ul style="list-style-type: none"> • Criteria for category I or II SIDS are not met. 	<ul style="list-style-type: none"> • Alternative diagnoses of natural or unnatural death are equivocal. 	<ul style="list-style-type: none"> • Autopsy has not been performed.

* Category IA includes infant deaths that meet the requirements of the general definition and also all of the requirements listed in the table.

†Category IB includes infant deaths that meet the requirements of the general definition and also meet all of the criteria for category IA except one or both of the listed ones - classic features of SIDS are present but incompletely documented.

‡Category II includes infant deaths that meet category I criteria except for ≥ 1 of the listed ones.

prenatal control, maternal smoking or alcohol and drug use during pregnancy, smoke in the infant's environment after birth, premature birth of a child, prone positioning during sleep, sleeping on a soft surface and/or with soft objects such as pillows or stuffed toys, bed-sharing with parents during sleep, overheating and head covering of infant, lack of breastfeeding (9). Since the first recommendations for supine placement of infants to prevent SIDS in 1992, SIDS postneonatal mortality rates declined 55% between 1992 and 2001 [14]. According to the medical statistics incidence of SIDS in our country is 5.9% [15].

Sudden unexplained death in childhood (SUDC) is the term used for an unexpected death of a child older than one year, which remains unexplained after a thorough examination of the case [16]. SUDC is less common than SIDS, and usually occurs between 1 and 4 years of age [5].

The causes of sudden death in children are often situations or events that could be prevented. Primary prevention includes implementation of measures to prevent the occurrence of a situation or condition that could lead to death, as well as the recognition of symptoms and signs that may precede the fatal outcome, while secondary prevention implies adequate and timely conduction of cardiopulmonary resuscitation [9, 17].

The aim of our study was to determine the most common cause of sudden death in pediatric patients admitted to the Clinic of Pediatrics of the Institute for Child and Youth Health Care of Vojvodina.

METHODS

The retrospective study was conducted at the Clinic of Pediatrics of the Institute for Child and Youth Health Care of Vojvodina in Novi Sad and included 49 patients, aged from 10 days to 17 years, in whom death occurred in the Emergency department and in the first 48 hours of hospitalization, in the period from 01.01.1995 to 31.12.2015. The cases of death in neonates hospitalized after birth in our Institute were excluded from our study. Data relevant to the occurrence of death were collected from the medical histories of patients: age and sex of the patient, symptoms that preceded the admission to the hospital, the circumstances of the event leading to death, date and time of hospital admission, previous illnesses, personal and family history, treatment before arrival in the hospital, diagnostics procedures (laboratory, radiological, neurophysiological) and treatment in hospital, date and time of death, diagnosis and autopsy findings.

RESULTS

In the period from 01.01.1995 to 31.12.2015 in the Emergency department and in the first 48 hours of hospitalization at the Clinic of Pediatrics of the Institute for Child and Youth Health Care of Vojvodina 124 deaths occurred. For 49 patients medical history was available, so they were included in our study (Figure 1). Due to the old age of medical histories, which were not stored electronically, a

part of the documentation, relating to the hospitalization of the patients in the Clinic of Pediatrics and from forensic medical institution, was not available.

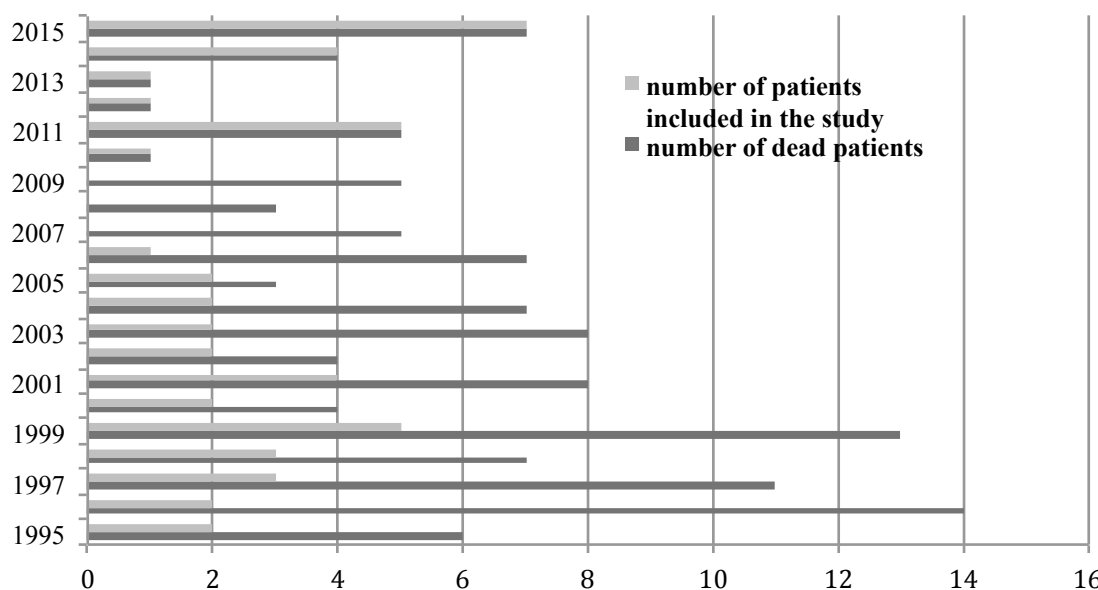


Figure 1. Distribution of patients by years.

Out of the total number of patients 30 (61%) were male and 19 (39%) were female. There were 3 newborns (6%), 21 infants (43%), 6 children aged 1 to 2 years (12%), 5 children aged 3 to 5 years (10%), 4 children aged 6 to 10 years (8%) and 10 children aged 11 to 18 years (21%) (Figure 2).

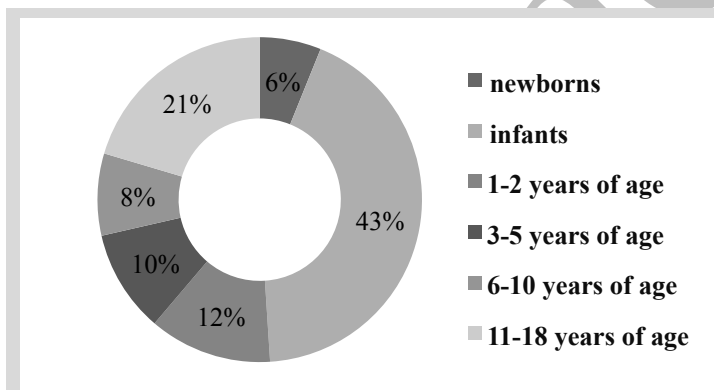


Figure 2. Distribution of patients by age.

Children who died were usually admitted to the hospital during the winter months (18 children (36%) from January to March) and at the end of the summer period (11 children (22%) in the period August - September). Patients came to our Institute more frequently during the weekend (on average 17% of patients per day during the weekend, compared to an average of 13% of patients per day during the working days), as well as in the evening and early morning hours (28 children (57%) from 18h to 6h).

In 9 patients (18%) before coming to the Institute cardiopulmonary resuscitation (CPR) was performed. In 23 patients (47%) certain therapeutic measures (antibiotics, anticonvulsants, cardiac therapy, inhaled therapy, oxygen therapy, parenteral hydration and antipyretics) were applied, while 17 patients (35%) received no therapy. CPR at the Institute was performed in 45 patients (92%). Eleven patients (22%) had previously been hospitalized for short period of time in other medical institutions.

Chronic disease was present in 22 patients (45%) and in 21 patients was associated with the cause of death. Only two children had oncological disease (pilocytic astrocytoma in neurofibromatosis

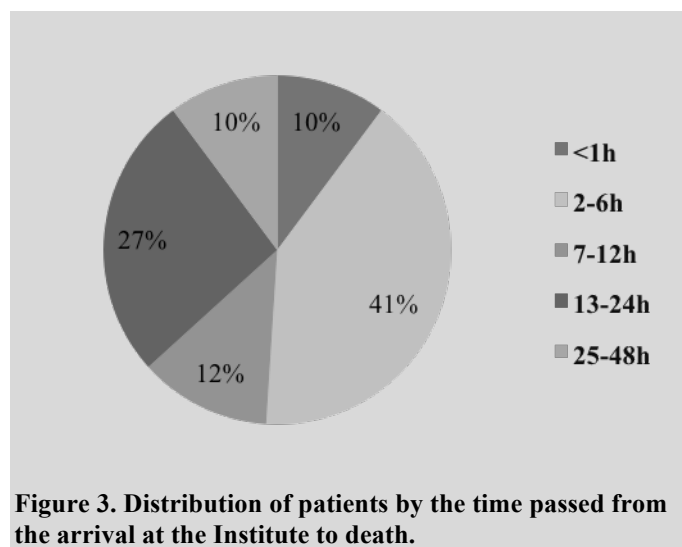


Figure 3. Distribution of patients by the time passed from the arrival at the Institute to death.

and one case of pineoblastoma). Ten children (20%) had a family history that could be associated with the cause of death.

In 25 patients (51%) death occurred within the first 6 hours after the arrival at the Institute (Figure 3). In 7 patients (14%) death occurred in the Emergency department, 34 patients (69%) died in the Intensive care unit, while 8 patients (17%) died in the others departments of the Institute.

Distribution of patients by the cause of death is presented in Table 3.

In 29 patients (59%) autopsy was conducted. For 17 patients (35%) the autopsy report was available and in that manner the cause of death was determined, while in others the cause of death was determined based on the medical history of the patient (anamnesis, clinical course and diagnostic procedures).

Table 3. Distribution of patients by the cause of death.

Cause of death and percentage share		Number of patients	Age
Infections (47%)	Meningococcal sepsis	5	From 4 months to 9 years
	Late neonatal sepsis and sepsis in infancy	5	3 newborns and 2 infants
	Enterocolitis and sepsis	5	From 2 months to 4,5 years
	Pneumonia, pneumonia and sepsis	7	From 5 months to 17 years
	Myocarditis	1	6 months
	Congenital heart defects	5	From 2 to 17 months
Heart failure (20%)	Paroxysmal supraventricular tachycardia	1	2 months
	Myocardial infarction	1	13 years
	Dilated cardiomyopathy	1	2,5 months
	Hypertrophic cardiomyopathy	1	7 years
Status epilepticus (8%)		1	5,5 months
Foreign body aspiration (8%)		4	From 5,5 months to 5 years
Diabetic ketoacidosis (2%)		4	From 2 months to 16 years
Rickets (2%)		1	15 years
Carbon monoxide poisoning (2%)		1	7,5 months
Hemolytic anemia (2%)		1	11 months
Suicide by hanging (2%)		1	9 years
Drowning (2%)		1	15 years
SIDS (2%)		1	2 years
SUDEP (2%)		1	2 months
		1	2 years

DISCUSSION

The definition of sudden death is quite variable, with different authors setting limits of zero, 1, 6 and 24 hours from the time of onset of symptoms and signs to the time of death. There is a reason for such a flexible approach, given that too rigid adherence to definitions is impractical and may lead to the exclusion of important disease entities. However, generally patients have either been completely well or have been suffering from only an apparently minor illness immediately before death. If a chronic illness was present it was thought to be stable. The common theme uniting all of these cases is that rapid deterioration occurred, culminating in death [3]. Unexpected death refers to the death of a child that was not anticipated as a significant possibility 24 hours before the death or where there was an unexpected collapse leading to or precipitating events that led to the death. This would also include unexpected death of a child with disabilities and/or chronic medical conditions [4].

In our study patients who died within the first 48 hours after the arrival at the Institute were included. In some cases death was declared at the Emergency department, while the other patients died within the first 48 hours of hospitalization. In 50% of patients death occurred within the first 6 hours from the arrival at the Institute, while in 90% of patients death occurred within 24 hours. The criterion of the first 48 hours was taken arbitrarily, in order to include the time period when the death that occurred could be called a sudden, whether it is due to acute disease, condition or accident, worsening of chronic disease or of unknown cause. Death which occurred in this period of time was certainly sudden and rapid, both for doctors and for parents, having in mind that most of these children came to the tertiary health institution from the outpatient environment with previously stable health condition, indicating no possible occurrence of death. A certain number of patients were transferred from other medical institutions where they were shortly hospitalized.

Seasonality of mortality and, in general, of disease is a well-known phenomenon in many countries worldwide. In addition to atmospheric effects, the seasonal pattern of mortality is shaped by non-atmospheric determinants such as environmental conditions or socioeconomic status [18]. Temperature differences are associated with mortality, but it is believed that the ability of people to protect themselves adequately from this is what predetermines the effect of temperature on the mortality of the population [19]. In developed countries, there is a higher mortality in the winter months, due to the predominance of respiratory diseases, while in tropical countries mortality is higher during the summer months, which is associated with high prevalence of intestinal infections [18]. It is observed that the effect of the time of year on mortality is especially strong in children, particularly in the first years of life, when they are most vulnerable to environmental factors. This phenomenon is the most prominent in rural areas [18, 20]. Although data on the seasonal distribution of sudden death in children are missing in the literature, we can conclude, based on our research, that they match the overall epidemiology of mortality in children in developed countries. In our study, the majority of children (36%) died in the first trimester of the year.

There are studies that indicate that the incidence of SIDS is more frequent on weekends compared to working days. Suggestions given for this finding are restricted access to medical care over the weekend, parents who might be more relaxed at the weekend, may pay less attention to children and may be less willing to seek medical help at the weekend for apparently minor illnesses. Some studies suggest sleep deprivation in children over the weekend as a possible factor that contributes to increased mortality, especially among uneducated mothers [21, 22]. In our study, more patients were admitted to hospital over the weekend compared to working days, while the largest number of them was received during the night, over a period of 18h-06h (57%).

In our study the predominance of male children is recorded (61%). It is known that mortality is higher in boys than girls in most parts of the world [23, 24]. This also applies to the sudden death [3]. This has been explained by sex differences in genetic and biological makeup, with boys being biologically weaker and more susceptible to diseases and premature death. These differences are particularly expressed in neonatal period and early infancy and are attributable to different sex chromosomes, as well as weaker immune systems due to the impact of male hormones [23, 24]. Recent studies have found that numerous preconception or prenatal environmental factors affect the probability of a baby being conceived male or female and that these factors can explain the differences in mortality between the sexes [23]. Serbia is among the countries where the sex difference in the mortality of infants is high, with a predominance of males [24].

Children are much more likely to die during the first year of life than they are at later ages. The risk of death gradually decreases with age, then again increases as they reach high school age [25]. This also applies to sudden death, taking into account that SIDS is 37 times more often than SUDC [5]. Our study included patients from neonatal age through adolescence. Newborns who were hospitalized at the Institute after birth were excluded from the study, because of the specificity of early neonatal period and pathology of these patients. Most patients in our study were infants (43%), which is in accordance with the literature.

Sudden unexpected death in the young is always a tragic and devastating event leaving the relatives not only with grief but also with the awareness that sudden death may strike the family again. Thus, if a young person dies suddenly and unexpectedly, an autopsy (including blood or tissue samples for the purpose of genetic testing) is required for the clinician to be able to manage the family in regard to inherited diseases. The study conducted in Denmark showed that despite operating under the same set of laws there were significant regional differences in forensic investigations of young persons suffering a sudden unexpected death [26]. Cases of incomplete and inadequate autopsies in children are also described in other publication [3]. Of the 49 patients included in our study 29 (59%) underwent autopsy and the autopsy report was available for 17 patients (35%). In patients in whom autopsy was not carried out the cause of death was established by doctor on the basis of anamnesis, clinical course of disease and diagnostic procedures.

When we talk about the analysis of the causes of sudden death in children we need to have in mind that our study included patients who died in the pediatric Emergency department and at the Clinic of Pediatrics of our Institute. This study did not include patients who died in surgical Emergency department and at the Clinic of Pediatric Surgery of our Institute. This indicates that trauma, as a possible cause of sudden death in children, was excluded from our study.

SIDS remains the most common cause of sudden and unexpected death in infancy despite dramatic falls in rates over the past decade. Over 1 year of age, the major causes of sudden natural death are malignancies, congenital anomalies and infections [3].

In our study, which included 21 infants, in only one case we can talk about SIDS. It was a male infant aged 2 months who was sleeping in bed with his mother. The autopsy could not determine a cause of death. Bed-sharing is a well known risk factor for SIDS. In this case we can also consider accidental suffocation as a kind of SUID-a, which in some cases is very difficult to distinguish from SIDS [9]. If we talk about the diagnosis of SIDS in this case, according to the San Diego definition it would be the category IB when SIDS is not fully documented due to lack of investigation of the scene where incidents leading to death occurred and caring out incomplete autopsy (which includes toxicological, microbiological, radiological analysis, chemical analysis of the vitreous body and metabolic screening) [13].

In high-income countries, mortality from infectious diseases in children and young people is uncommon. Occasionally, the clinical course of the infectious disease is atypical and very aggressive and death occurs suddenly. Sudden unexpected death from infectious disease (SUDID) accounts for 10 to 30% of all sudden deaths in children. SUDID incidence is especially high in infants as their immune system is still developing. The most common infections that lead to sudden death among children and young people are myocarditis, respiratory infections and invasive meningococcal infections [6]. In accordance with the literature in our study the largest number of deaths was due to infection (47%). Systemic bacterial infection (83%) was the most frequent cause. There were also 3 cases of pneumonia and one case of myocarditis.

Cardiovascular diseases are together with infections a major cause of sudden deaths in children [3]. Although all deaths result in asystole, not all sudden deaths are caused by arrhythmias [2]. Sudden cardiac death (SCD) is defined as death that is abrupt, unexpected and due to cardiovascular cause. It is generally recognized as death that occurs within 1 hour from the onset of cardiovascular symptoms. In young people it typically occurs within a few minutes of symptom onset. Etiology of SCD can be divided into two categories: arrhythmic and non-arrhythmic, with hypertrophic cardiomyopathy being the commonest. Approximately 20-25% of SCD occur during sports activities [7]. In our study there were 10 sudden cardiac deaths (20%).

Patients with epilepsy, including children, have an increased mortality rate compared with the general population. Most cases of death among these children can be attributed to the underlying neurological disease, but some are epilepsy related, including accidents, drowning, status epilepticus

and SUDEP [27]. Definition of SUDEP is written in Table 1. The exact pathophysiology of SUDEP is currently unknown [8]. SUDEP is less common among children than among adults. Children with severe epilepsy and comorbid conditions are at a higher risk [28]. In our study there was one case of SUDEP. It was a boy aged 2 years with chronic disease (epileptic encephalopathy, severe mental retardation, amaurosis and atrophy of the optic nerve) who stopped breathing at home, 20 minutes before arrival at the Institute.

Status epilepticus is a rare but serious condition that is fatal in about 1% of children. The incidence is the highest in children under one year of age [29]. The most common causes of status epilepticus are atypical febrile seizures, metabolic abnormalities, central nervous system infections, brain tumors, cerebral dysgenesis, changes in dose of antiepileptic drugs and drug overdose [30]. In our study there were 4 patients who died due to epileptic status of different etiology. Although the majority of deaths in patients who have malignancies are expected in some cases such a death can be sudden, if it occurs earlier than expected or under unexplained circumstances [4]. In our study there was boy with pineoblastoma, aged 3 years, who died due to recurrent seizures caused by progression of disease despite the oncological treatment.

Choking is a leading cause of morbidity and mortality among children, especially those who are 3 years of age or younger. The main reasons for this are the characteristics of the child's airway, the underdeveloped ability to chew and swallow food, still insufficiently developed cough reflex and the tendency of small children to explore their environment by putting various objects in his mouth. Children with swallowing disorder caused by neuromuscular disease, developmental delay and other conditions are at increased risk of a foreign body aspiration [31]. Our study recorded four deaths after aspiration of a foreign body - food. The patients were two infants, a boy aged 14 years with cerebral palsy and adolescent girl aged 16 years.

Rickets is a major health problem in many countries around the world. It is mainly caused by a lack of vitamin D and can lead to hypocalcemic seizures, cardiac arrest and sudden death of a child [32]. Our study included a seven-month old infant who died due to hypocalcemic tetany caused by rickets.

Evans syndrome is the association of immune thrombocytopenic purpura (ITP) and autoimmune hemolytic anemia (AIHA) mediated by autoantibodies and the diagnosis is made after excluding other diseases. Bicitopenia can occur at the same time or at different periods of time. This syndrome has a mortality rate of 10 to 36%, and the main causes of death are hemorrhage and infection [33]. In our study we considered this diagnosis in a boy aged 9 years with recurrent thrombocytopenia and acute hemolytic anemia.

Even in developed countries, some 15–70% of all newly diagnosed children with diabetes present with diabetic ketoacidosis (DKA). Cerebral edema occurs in 0.5-1% of all episodes of DKA in children and is the most common cause of mortality in children with DKA [34]. In our study, death due to DKA occurred in adolescent girl aged 15 years.

Carbon monoxide (CO) is a toxic, colorless, odorless gas which is a product of incomplete combustion of gas, coal, wood and petrol. The largest number of poisoning happens at home. Children and the elderly are at higher risk for poisoning by this gas compared to healthy adults [35, 36]. In our study there was a single case of CO poisoning, which resulted in a fatal outcome.

In most countries in the world drowning is one of the three most common causes of death from unintentional injury, with the highest rate in children under 5 years of age [37]. In our study there was a single case of a boy aged 2 years who drowned in a cesspool.

In 2012 an estimated 1.3 million adolescents died around the world. The leading causes of death among adolescents in 2012 were road injury, HIV, suicide, lower respiratory tract infections and interpersonal violence [38]. In our study there was a single case of suicide by hanging in adolescent boy aged 15, who was found by his mother hanging on the water supply pipe in the bathroom.

Despite the fact that medical crisis started before the arrival of patients at the Institute in only 18% of them CPR was performed before hospital admission, while 35% of patients received no therapy. Many pediatric emergencies are managed primarily by providers who are not pediatric specialists and who have limited pediatric emergency medical experience. Therefore, it is necessary to educate them in terms of timely and adequate care of life-threatened children, in accordance with the latest recommendations [39].

CONCLUSION

Our study shows that infants are at the highest risk of sudden death, while the most frequent causes of death are infections and cardiovascular diseases. Sudden death in children can be prevented in the most cases. Gaining insight into the structure of sudden death in children gives us opportunity to promote preventive measures and highlights the need for health education of parents and timely diagnosis and therapy in both pre-hospital and intra-hospital care of life-threatened patients.

REFERENCES

1. O'Malley P, Barata I, Snow S; American Academy of Pediatrics Committee on Pediatric Emergency Medicine; American College of Emergency Physicians Pediatric Emergency Medicine Committee; Emergency Nurses Association Pediatric Committee. Death of a child in the emergency department. *Pediatrics*. 2014;134(1):e313–30.
2. Wren C. Sudden death in children and adolescents. *Heart*. 2002; 88: 426–31.
3. Byard RW. Sudden death in the young. 3th ed. Cambridge: Cambridge University Press; 2010.
4. Pan-Cheshire Local Safeguarding Children Board (LSCB) Guidelines (Cheshire East, Cheshire West & Chester, Halton and Warrington) Pan-Cheshire Guidelines for The Management of Sudden Unexpected Death in Infants and Children (SUDIC) 2015. [Cited 2016 Dec 14]. Available from: http://www.proceduresonline.com/LimitedCMS_centrally_managed_content/pancheshire/shared_files/pan_cheshire_lscb_guidelines_for_sudi.pdf
5. McClain M. Sudden unexpected infant and child death: A guide for emergency department personnel. Boston, MA: Massachusetts Center for Sudden Infant Death Syndrome 2008. [Cited 2016 Dec 14]. Available from: <http://www.bmc.org/Documents/bmcSIDSguideforEDpersonnel.pdf>
6. Morentin B, Suárez-Mier MP, Aguilera B, Arrieta J, Audicana C, Fernández-Rodríguez A. Clinicopathological features of sudden unexpected infectious death: population-based study in children and young adults. *Forensic Sci Int*. 2012; 220(1–3): 80–4.

7. Gajewski KK, Saul JP. Sudden cardiac death in children and adolescents (excluding sudden infant death syndrome). *Ann Pediatr Cardiol*. 2010; 3(2): 107–12.
8. Maguire MJ, Jackson CF, Marson AG, Nolan SJ. Treatments for the prevention of sudden unexpected death in epilepsy (SUDEP). *Cochrane Database Syst Rev*. 2016; 19(7): CD011792.
9. AAP task force on sudden infant death syndrome. SIDS and other sleep-related infant deaths: updated 2016 recommendations for a safe infant sleeping environment. *Pediatrics*. 2016; 138(5): e20162938.
10. Shapiro-Mendoza CK, Camperlengo L, Ludvigsen R, Cottengim C, Anderson RN, Andrew T, et al. Classification system for the sudden unexpected infant death case registry and its application. *Pediatrics*. 2014; 134(1): e210–9.
11. Willinger M, James LS, Catz C. Defining the sudden infant death syndrome (SIDS): deliberations of an expert panel convened by the National Institute of Child Health and Human Development. *Pediatr Pathol*. 1991; 11(5): 677–84.
12. Đurić M. Sindrom iznenadne smrti odojčeta. In: Bogdanović R, Radlović N, editors. *Pedijatrija*. Beograd: Akademska misao; 2016. p. 1715–8.
13. Krous HF, Beckwith JB, Byard RW, Rognum TO, Bajanowski T, Corey T, et al. Sudden infant death syndrome and unclassified sudden infant deaths: a definitional and diagnostic approach. *Pediatrics*. 2004;114:234-8. [PMID: 15231934]
14. Malloy MH, MacDorman M. Changes in the classification of sudden unexpected infant deaths: United States, 1992–2001. *Pediatrics*. 2005; 115(5): 1247–53.
15. Lozanović-Miladinović D. Urgentna stanja u strukturi morbiditeta i mortaliteta dece i adolescenata. In: Janković B, Milenković A, Milovanović D, editors. *Urgentna pedijatrija u vanbolničkim uslovima: priručnik za lekare primarne zdravstvene zaštite*. Beograd: UNICEF; 2002. p. 11–5.
16. Krous HF, Chadwick AE, Crandall L, Nadeau-Manning JM. Sudden unexpected death in childhood: a report of 50 cases. *Pediatr Dev Pathol*. 2005; 8(3): 307–19.
17. Berger S, Maccalli E. Strategies for the prevention of sudden cardiac death in children and adolescents. *Pediatr Ann*. 2015; 44(12): e292–7.
18. Burkart K, Khan MH, Krämer A, Breitner S, Schneider A, Endlicher WR. Seasonal variations of all-cause and cause-specific mortality by age, gender, and socioeconomic condition in urban and rural areas of Bangladesh. *Int J Equity Health*. 2011; 10(1): 32.
19. Gemmell I, Mcloone P, Boddy FA, Dickinson J, Watt GCM. Seasonal variation in mortality in Scotland. *Int J Epidemiol*. 2000;29(2):274-9. [PMID: 10817125]
20. Mutisya M, Orindi B, Emina J, Zulu E, Ye Y. Is mortality among under-five children in Nairobi slums seasonal? *Trop Med Int Health*. 2010;15(1):132-9.
21. Mooney JA, Helms PJ, Jolliffe IT. Higher incidence of SIDS at weekends, especially in younger infants. *Arch Dis Child*. 2004; 89: 670–2.
22. Spiers PS, Guntheroth WG. The effect of the weekend on the risk of sudden infant death syndrome. *Pediatrics*. 1999; 104(5): e58.
23. Pongou R. Why is infant mortality higher in boys than in girls? A new hypothesis based on preconception environment and evidence from a large sample of twins. *Demography*. 2013; 50: 421–44.
24. United Nations, Department of Economic and Social Affairs, Population Division. Sex differentials in childhood mortality. 2012. United Nations publication, ST/ESA/SER.A/314. [cited 2016 Dec 14]. Available from: <http://www.un.org/esa/population/publications/SexDifChildMort/SexDifferentialsChildhoodMortality.pdf>
25. Child Trends. Infant, child, and teen mortality. 2016. [cited 2016 Dec 14]. Available from: http://www.childtrends.org/wp-content/uploads/2016/11/63_Child_Mortality.pdf
26. Winkel BG, Holst AG, Theilade J, Kristensen IB, Thomsen JL, Bayer I, et al. Differences in investigations of sudden unexpected deaths in young people in a nationwide setting. *Int J Legal Med*. 2012; 126: 223–9.
27. Grønberg S, Uldall P. Mortality and causes of death in children referred to a tertiary epilepsy center. *Eur J Paediatr Neurol*. 2014;18(1):66-71.
28. Donner EJ. Sudden unexpected death in epilepsy: Who are the children at risk? *Paediatr Child Health*. 2014;19(7):389. [PMID: 25332679]
29. Loddenkemper T, Syed TU, Ramgopal S, Gulati D, Thanaviratnanich S, Kothare SV, et al. Risk factors associated with death in in-hospital pediatric convulsive status epilepticus. *PLoS One*. 2012; 7(10): e47474.
30. Shah S, Shah N, Johnson R, West AN, Prasad N. Single center outcomes of status epilepticus at a pediatric intensive care unit. *Can J Neurol Sci*. 2016; 43(1): 105–12.
31. Committee on Injury, Violence, and Poison Prevention, American Academy of Pediatrics. Policy statement: Prevention of choking among children. *Pediatrics*. 2010; 125: 601–7.

32. Scheimberg I, Perry L. Does low vitamin D have a role in pediatric morbidity and mortality? An observational study of vitamin D in a cohort of 52 postmortem examinations. *Pediatr Dev Pathol*. 2014; 17(6): 455–64.
33. Aladjidi N, Fernandes H, Leblanc T, Vareliette A, Rieux-Laucat F, Bertrand Y, et al. Evans syndrome in children: long-term outcome in a prospective French national observational cohort. *Front Pediatr*. 2015; 3:79.
34. Wolfsdorf J, Glaser N, Sperling MA; American Diabetes Association. Diabetic ketoacidosis in infants, children, and adolescents: A consensus statement from the American Diabetes Association. *Diabetes Care*. 2006; 29(5): 1150–9.
35. Sircar K, Clower J, Shin MK, Bailey C, King M, Yip F. Carbon monoxide poisoning deaths in the United States, 1999 to 2012. *Am J Emerg Med*. 2015; 33(9): 1140–5.
36. Fisher DS, Bowskill S, Saliba L, Flanagan RJ. Unintentional domestic non-fire related carbon monoxide poisoning: data from media reports, UK/Republic of Ireland 1986–2011. *Clin Toxicol (Phila)*. 2013; 51(5): 409–16.
37. World Health Organization. World report on child injury prevention. Geneva, WHO, 2008.
38. World Health Organization. Global health estimates for deaths by cause, age, and sex for years 2000–2012. Geneva: WHO, 2014.
39. Maconochie IK, Bingham R, Eich C, López-Herce J, Rodríguez-Núñez A, Rajka T, et al. European Resuscitation Council Guidelines for Resuscitation 2015: Section 6. Paediatric life support. *Resuscitation* 2015; 95: 223–48.