Swiss Paediatric Surveillance Unit Report 2021 / 2022

SWISS PAEDIATRIC SURVEILLANCE UNIT

This biennial report of the SPSU covers the period 2021 – 2022. The joint work of 29 pediatric clinics in Switzerland, cooperating in this unique framework with the Federal Office of Public Health FOPH and the paediatric switzerland since 1995, was exposed to additional stress factors due to the COVID-19 pandemic during the reporting period. Despite the considerable additional demands of dealing with this challenging situation, the SPSU partners once again did an excellent job.

The card return rate for reporting all studies in 2021 / 2022 was again 100 %, underscoring the representative nature of the study setting within SPSU. A very sincere thank you to all who contributed to this success.

The pandemic reaffirmed the importance of structures such as the SPSU. The SARS-CoV-2 study – initiated in March 2020, immediately after the start of the pandemic, and co-led by Nicole Ritz and Petra Zimmermann – provided valuable data and led to several publications. Without the existing SPSU network, a representative, epidemiologically necessary study of this kind would not have been possible to be set up so rapidly.

The participating hospitals coped excellently with the high reporting burden of this study.

Synergies are demonstrated by the current studies on invasive Group A streptococcal infections and varicella-zoster virus-associated hospitalisations since VZV infection increases the risk of secondary skin or mucosal infection.

Across all studies, the total number of reports submitted was 1077 in 2021 and 2845 in 2022.

I want to express special thanks to Daniela Beeli, Mirjam Mäusezahl and Fabian Tschaggelar at the FOPH. They are largely responsible for the quality of reporting and data. Through their tireless support and communication with various SPSU partners, they contribute to the operation of SPSU as a constructive unit. On behalf of the SPSU Steering Committee, many thanks.

New studies within the SPSU are always welcome. We are happy to provide advice on questions concerning protocol and feasibility.

Dr Andreas Wörner
Chair of the SPSU Steering Committee

In 2021 and 2022, the Swiss Paediatric Surveillance Unit (SPSU) received the following reports of confirmed cases:

2021: a total of 582 of confirmed cases from 29 participating paediatric teaching hospitals (see Box) for six ongoing studies: 521 cases of SARS-CoV-2, 25 of congenital cytomegalovirus, 17 cases of invasive group A streptococcal infection, 10 cases of varicella-zoster-virus associated hospitalisation, 8 of acute flaccid paralysis as a polio surveillance indicator and 1 of vitamin K deficiency bleeding.

2022: a total of 915 of confirmed cases from 29 participating paediatric teaching hospitals (see participating hospitals) for seven ongoing studies: 680 cases of SARS-CoV-2, 104 of invasive group A streptococcal infection, 81 cases of varicella-zoster-virus associated hospitalisation, 34 of congenital cytomegalovirus, 9 of acute flaccid paralysis as a polio surveillance indicator, 2 of vitamin K deficiency bleeding and 0 cases of acute paediatric hepatitis of unknown origin.

1. General information about the SPSU

The Swiss Paediatric Surveillance Unit (SPSU)[1] is a notification system for monitoring rare paediatric diseases and rare complications of more common illnesses among children under 16 who are hospitalised in Switzerland (Zimmermann et al. Soz Präventivmed 1995; 40: 392 – 5). The SPSU is operated by paediatric switzerland and the Federal Office of Public Health (FOPH).

The notification system is:

- simple, as it involves minimal effort;
- flexible, as it permits rapid investigation of emerging epidemiological issues;
- comprehensive, as cases meeting the case definition are actively identified in every hospital;
- nationally representative, as all of Switzerland's paediatric hospitals participate.

The SPSU is designed to promote research on rare paediatric diseases and to monitor epidemiological trends. Worldwide, there are nine comparable data collection systems – in Australia, Belgium, Canada, England, Germany, Ireland, the Netherlands, New Zealand and Wales. These countries collaborate and share experience through the International Network of Paediatric Surveillance Units (INoPSU), www.inopsu.com (see "International activities").

The results of individual studies are also regularly published in scientific journals (see the list of publications). Guidelines on the inclusion of the SPSU in the list of authors and acknowledgements are available online at: www.spsu.ch. Proposals for new studies are to be addressed to the Chair of the SPSU Committee, Dr A. Wörner (Senior Physician, UKBB, Spitalstrasse 33, CH-4056 Basel, andreas.woerner@ukbb.ch). A description of the surveillance system and guidelines for the inclusion of studies are available from the SPSU secretariat [Communicable Diseases Division, FOPH, CH-3003 Bern, and Tel. +41 (0)58 463 87 06, spsu@bag.admin.ch] or online at: www.spsu.ch.

2. International activities

Through its participation in International Network of Paediatric Surveillance Units (INoPSU), the SPSU enables studies involving international collaboration. The INoPSU provides researchers and interested parties with simple and low-threshold access to study protocols from other countries operating national surveillance systems comparable to the SPSU (www.inopsu.com). This offers a globally unique opportunity to compare demographic, diagnostic, clinical and therapeutic data on rare paediatric diseases.

Every two to three years, representatives from the 10 current member states meet to share the latest findings at a scientific conference. Since the start of the pandemic, these exchanges have become more frequent, taking the form of regular online meetings.

1 SPSU Committee: A. Wörner, Basel (Chair); C. Hagmann, Zurich; I. Bolt, Bern; B. Laubscher, Neuchâtel and Lausanne; G. Simonetti, Bellinzona; F. Stollar, Geneva; M. Mäusezahl, Bern; D. Beeli, Bern; F. Tschaggelar, Bern.

The activities of INoPSU are illustrated by the following publications (listed in reverse chronological order):

– Abu Raya B, Jost M, Bettinger J A, Bortolussi R, Grabowski J, Lacaze-Masmonteil T, Robinson J L, Posfay-Barbe K M, Galanis E, Schutt E, Mäusezahl M, Kollmann T R. Listeriosis in infants: Prospective surveillance studies in Canada and Switzerland, Paediatrics & Child Health, 2021; https://doi.org/10.1093/pch/pxab035
– Katzman DK, Madden S, Nicholls D, Mawjee K, and Norris ML. From questions to answers: Examining the role of pediatric surveillance units in eating disorder research. Int J Eat Disord. 2017 Mar;50(3):259-265. Doi: 10.1002/eat.22663. Epub 2017 Jan 17.
– Desai S, Smith T, Thorley BR, Grenier D, Dickson N, Altpeter E, SPSU Committee, Sabbe M, Elliott E, Zurynski Y. Performance of acute flaccid paralysis surveillance compared with World Health Organization standards. Paediatr Child Health. 2015;51(2):209–14. https://doi.org/10.1111/jpc.12691
– Grenier D, Lynn R, Zurynski Y. on behalf of all national paediatric surveillance unit investigators. Public health impacts of the International Network of Paediatric Surveillance Units. Paediatr Child Health. 2009;14(8):499–500. http://doi.org/10.1093/pch/14.8.499
– Grenier D, Elliott EJ, Zurynski Y, Pereira R, Reece M, Lynn R, von Kries R. Beyond counting cases: Public health impacts of national Paediatric Surveillance Units. Arch Dis Child. 2007;92(6):527–55. http://dx.doi.org/10.1136/adc.2006.097451

3. Participating hospitals

Pädiatrische Klinik, Kantonsspital, **Aarau**; Pädiatrische Klinik, Kantonsspital, **Baden**; Universitäts-Kinderklinik beider Basel, UKBB, **Basel**; Istituto Pediatrico della Svizzera Italiana, **Bellinzona**; Universitätsklinik für Kinderheilkunde, **Bern**; Neonatologie, Universitätsklinik für Kinderheilkunde, **Bern**; Kinderspital Wildermeth, **Biel**; Klinik für Kinder und Jugendmedizin, Kantonsspital, **Chur**; Service de Pédiatrie, Hôpital du Jura, **Delémont**; Service de Pédiatrie, Hôpital Cantonal, **Fribourg**; Hôpital des Enfants, HUG, **Genève**; Service de Pédiatrie, CHUV, **Lausanne**; Hôpital de l'Enfance, **Lausanne**; Division de Néonatologie, CHUV, **Lausanne**; Pädiatrische Klinik, Kantonsspital, **Luzern**; Service de Pédiatrie, Hôpital de Zone, **Morges**; Klinik für Kinder und Jugendliche, Kantonsspital, **Münsterlingen**; Département de Pédiatrie, Hôpital Pourtalès, **Neuchâtel**; Service de Pédiatrie, Centre hospitalier, **Rennaz**; Neonatologie, Klinik für Geburtshilfe und Gynäkologie, **St. Gallen**; Pädiatrische Klinik, Ostschweizer Kinderspital, **St. Gallen**; Service de Pédiatrie, CHCVs, **Sion**; Pädiatrische Klinik, Spitalzentrum Oberwallis, **Visp**; Kinderklinik, Kantonsspital, **Winterthur**; Service de Pädiatrie, eHnV, **Yverdon**; Pädiatrie / Neonatologie, **Zollikerberg**; Universitäts-Kinderklinik, **Zürich**; Klinik für Kinder und Jugendliche, Spital Triemli, **Zürich**; Neonatologie, Universitäts-Frauenklinik, **Zürich**.

4. Overview of the surveillance years 2021/2022

As in previous years, all paediatric teaching hospitals took part in the SPSU survey in 2021 and 2022. Once again, the return rate for report cards was 100%, i.e. all hospitals complied with their monthly notification responsibilities **(Tables 1 and 2)**.

In 2021, a total of 1077 cases were reported by 28 hospitals. Of these, 582 were classified as confirmed cases, while 17 cases did not meet the case definitions or were identified as duplicate reports. Information for classification was missing in 474 cases. One paediatric hospital reported no cases of the diseases under surveillance during this period.

In 2022, a total of 2845 cases were reported by 29 hospitals. Of these, 910 were classified as confirmed cases, while five cases did not meet the case definitions or were identified as duplicate reports. Information for classification was missing in 1929 cases.

Table 1 – SPSU 2021: Overview of reported cases and report card return rate

Study	No. of cases reported to SPSU	Card return rate (%)	Total no. of cases	Confirmed cases	Not confirmed	Data unavailable / questionnaires not received
Acute flaccid paralysis	10	100	10	8	0	2
Congenital cytomegalovirus	30	100	28	25	2	3
Invasive Group A streptococcal infection	18	100	18	17	0	1
SARS-CoV-2 infections	1004	100	536	521	15	468
Varicella-zoster virus	14*	100	10	10	0	0
Vitamin K deficiency bleeding	1	100	1	1	0	0

*Study started July 1st, 2021.

Table 2 – SPSU 2022: Overview of reported cases and report card return rate

Study	No. of cases reported to SPSU	Card return rate (%)	Total no. of cases	Confirmed cases	Not confirmed	Data unavailable / questionnaires not received
Acute flaccid paralysis	13	100	13	9	0	4
Acute paediatric hepatitis of unknown origin	11*	100	11	0	1	10
Congenital cytomegalovirus	55**	100	51	34	0	21
Invasive Group A streptococcal infection	112	100	112	104	0	8
SARS-CoV-2 infection	2568	100	682	680	2	1886
Varicella-zoster virus	82	100	81	81	0	0
Vitamin K deficiency bleeding	4	100	4	2	2	0

*Study started July 1st, 2022. Previously occurring cases in the period from March 1st, 2022 to June 30th, 2022: 5
**Study ended on March 31st, 2023. Number of reports and cases from January to March 2023 are included.

Table 3 – Ongoing and completed SPSU studies

	Duration	confirmed cases
Ongoing studies		
Acute flaccid paralysis	1/1995 (ongoing)	302
Invasive Group A streptococcal (iGAS) infection	12/2017 (ongoing)	228
Vitamin-K deficiency bleeding	9/2018 (ongoing)	6
Varicella-zoster virus-associated hospitalisations (Including post-infectious complications)	7/2021 (ongoing)	91
Acute paediatric hepatitis of unknown origin	7/2022 (ongoing)	0
Completed studies		
SARS-CoV-2 infections	4/2020 – 3/2023	2085
Congenital cytomegalovirus	4/2016 – 3/2023	185
Neonatal listeriosis	6/2017 – 12/2020	9
Pertussis	4/2006 – 3/2010 and 1/2013 – 12/2020	323
Tuberculosis	12/2013 – 11/2019	138
Kawasaki disease	3/2013 – 2/2019	331
Symptomatic congenital toxoplasmosis	1/1995 – 12/1998 and 6/2009 – 5/2017	21
Congenital rubella	1/1995 – 12/2016	2
Urea cycle disorder	1/2012 – 12/2015	5
Mycoplasma pneumoniae encephalitis	7/2013 – 06/2015	0
Extended-spectrum beta-lactamase (ESBL)-producing Gram negative bacilli	7/2008 – 6/2012	403
Severe hyperbilirubinaemia	10/2006 – 12/2011	172
Vitamin K deficiency bleeding	1/1995 – 12/2000 and 7/2005 – 6/2011	27
Acute rheumatic fever	6/2000 – 5/2010	24
Anaphylaxis	5/2007 – 4/2010	58
Haemolytic-uraemic syndrome	4/1997 – 3/2003 and 4/2004 – 3/2010	249
Neonatal herpes	7/2002 – 6/2008	5
Neural tube defects	1/2001 – 12/2007	258
Shaken baby syndrome	7/2002 – 6/2007	50
Intussusception	4/2003 – 3/2006	243
Severe RSV infections	10/2001 – 9/2005	462
Varicella-zoster virus infection	1/2000 – 3/2003	235
Tick-borne encephalitis	3/2000 – 2/2003	23
Cystic periventricular leukomalacia	1/1996 – 12/1997	48

4. Results of ongoing studies

4.1 Acute flaccid paralysis

Background

Poliomyelitis, formerly known as infantile paralysis, is a viral disease that can result in lifelong disability and even death. In 1988, the World Health Organization (WHO) therefore set itself the goal of eradicating polio worldwide. Switzerland had already achieved this goal in 1983, when the last case of wild-type poliovirus was recorded by the Federal Office of Public Health (FOPH).

In 2002, the WHO declared the entire WHO European Region (including Switzerland) polio-free. The FOPH has to provide evidence of this status to the WHO every year. For the WHO, detection of cases of acute flaccid paralysis where poliomyelitis can be excluded provides evidence of active polio surveillance. To supplement the mandatory notification system for polio, surveillance of acute flaccid paralysis (AFP) was established as part of the SPSU in Switzerland in 1995.

The WHO has defined two indicators for evaluating the sensitivity of surveillance:

- the annual non-polio AFP rate should be at least 1 per 100'000 in children under 15;
- the proportion of AFP cases where two stool specimens are collected 24 – 48 hours apart for poliovirus testing should be at least 80%.

Aims of the study

- To provide evidence that Switzerland is polio-free and
- To raise awareness of poliomyelitis among the medical profession.

All AFP cases are to be investigated for poliovirus infection [1], thus providing a description of the epidemiological, clinical and microbiological characteristics of AFP.

Case definition

Clinical symptoms in a child under 16:

- acute onset of flaccid paralysis in one or more limbs with decreased or absent tendon reflexes or
- acute onset of bulbar paralysis.

Results

The inclusion criteria for the study do not fully match those of the WHO. The SPSU includes children under 16, whereas the WHO guidelines specify children under 15. This report therefore only includes AFP cases in children under 15. In 2021, 10 cases of AFP were reported, of which 8 met the case definition criteria. The annualised AFP rate was therefore 0.54 cases per 100'000 population. In 4 cases, at least one stool specimen was tested. In 2022, 13 cases of AFP were reported, of which 9 met the case definition criteria. The annualised AFP rate was therefore 0.60 cases per 100'000 population. Stool specimens were tested for polio or enteroviruses in 5 cases.

As in previous years, Switzerland failed to meet the WHO sensitivity requirements in both 2021 and 2022 **(Table 4)**, with not enough stool specimens being tested for enteroviruses or polioviruses.

Conclusions

The spread of any imported polioviruses must be avoided in all circumstances. Therefore, in accordance with WHO guidelines, the FOPH recommends the following measures:

- achieve a high level of vaccination coverage;
- high-quality active surveillance to ensure rapid detection of any imported polioviruses or circulating vaccine-derived viruses;
- secure storage and safe handling of polioviruses at laboratories with an appropriate biosafety level.

As Switzerland does not fulfil the quality requirements specified by the WHO with regard to stool testing, more efforts will be made to inform hospitals of the need to test at least one stool specimen for polioviruses in all cases meeting the inclusion criteria. In view of the high quality of Swiss laboratories, the FOPH considers the testing of one stool specimen to be

adequate. The costs will be borne by the FOPH. Stool specimens are to be sent to the National Polio Reference Laboratory (Institute for Medical Microbiology, Petersplatz 10, CH-4003 Basel).

Polio vaccination is recommended for all non-immunised individuals regardless of age. People travelling to polio-endemic regions should check their immunity status and obtain any booster or catch-up vaccinations required. In 2022, Afghanistan and Pakistan were classified as polio-endemic countries.

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Table 4 – Data since 2010: confirmed cases of acute flaccid paralysis (AFP) in children <15 years

Year	Total AFP cases (<15 years)	Total "non-polio" AFP cases	AFP case rate per 100,000	Total AFP cases with 1/2 stool specimens	% of AFP cases with ≥ 1 stool specimen tested
2022	9	9	0.60	4/1	59
2021	8	8	0.54	4/0	50
2020	4	4	0.29	0/0	0
2019	12	12	0.86	4/4	67
2018	16	16	1.3	9/0	56
2017	8	8	0.6	2/0	25
2016	25	25	1.9	12/2	56
2015	8	8	0.7	1/2	38
2014	9	9	0.7	2/0	22
2013	9	9	0.7	0/1	11
2012	8	8	0.7	1/5	75
2011	3	3	0.3	2/2	67
2010	9	9	0.8	5/4	55

4.2 Congenital cytomegalovirus

Background

Cytomegalovirus (CMV) infection is caused by a virus from the Herpesviridae family. It is a widespread infection in children and adults that is inapparent to mild at the start of the infection, with a seroprevalence of approximately 80% worldwide but varies greatly by geographic region between 40% and 100% [1,2]. In immunocompromised patients, CMV is a significant cause of increased morbidity and mortality. It is the most common congenital infection, with an average prevalence of 1% of live births worldwide. This prevalence also varies by geographic region and is between 0.2% to 6.1% of live births in developing countries [1,2,3,5]. Infection in the first or second trimester of pregnancy can result in abnormalities in the child.

Approximately 10% to 15% of affected newborns display symptoms at birth with the following clinical symptoms: thrombocytopenia, hepatitis, hepatosplenomegaly, chorioretinitis, microcephaly, intrauterine growth restriction. Sensorineural and developmental sequelae are observed in half of all children with symptoms at birth, but also in 14% of children who are infected but asymptomatic at birth [1,3,5].

Systematic screening for maternal seroconversion during pregnancy is not currently recommended in Switzerland (gynécologie suisse, expert letter no. 47) or worldwide [5], as it is virtually impossible to prevent CMV from being transmitted to the fetus. Biologically, it is very difficult to distinguish between a first infection and reinfection or reactivation, and maternal immunity prior to pregnancy does not protect against reinfection or reactivation; two-thirds of infected newborns are from mothers who were CMV-seropositive at the start of pregnancy [4,5].

Information and hygiene recommendations for pregnant women are currently the most important CMV infection prevention strategy. The role of vaccines and antivirals remains unclear [6].

Aims of the study

No data on congenital CMV (cCMV) infections are currently available in Switzerland. However, it is important to obtain data on diagnosis and on primary and secondary morbidity so as to allow recommendations to be made for screening and treatment. Since April 1st, 2016, an SPSU study has been collecting data on confirmed and suspected cCMV cases.

The study is designed to measure and track the prevalence of live births with confirmed cCMV infection. In addition, a national registry is to be established for epidemiological monitoring, and the effects of this congenital infection on psychomotor development are to be determined.

The study could further be used to examine the possibility of organising systematic cCMV screening at birth, and to determine the socio-demographic characteristics of these patients in Switzerland.

Case definition

Confirmed cCMV cases: newborns with an in utero or ex utero diagnosis of cCMV by PCR before 3 weeks of age (amniotic fluid, cord blood, infant's blood/urine), direct isolation of CMV by culture or antigen detection.

Suspected cCMV cases: positive IgM serology test or isolation of CMV by PCR (blood, urine) after 3 weeks of age, but before 1 year of age, with symptoms consistent with cCMV (premature birth, microcephaly, intracranial calcifications, etc.)

Results

In 2021, 28 confirmed cases were recorded, i.e. 2.6 cases per 10'000 births (89'644 births in Switzerland in 2021).

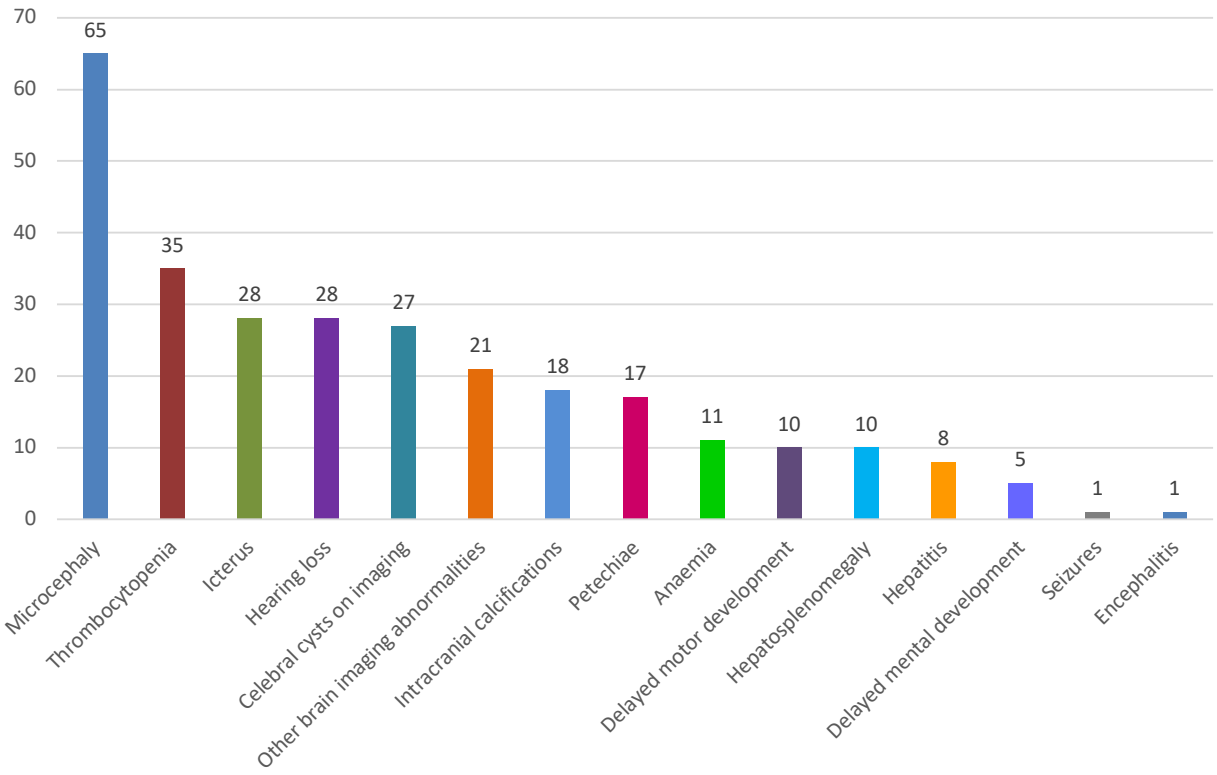
An increase in incidence was observed in 2022, 37 cases i.e. 4.5 per 10'000 births were recorded (82'045 births in Switzerland in 2022).

In the first quarter of 2023, 14 cases were reported to SPSU (no data are available on the number of births in the first quarter of 2023).

The recording of data began on April 1st, 2016 and ended on March 31st, 2023. Data collection for patients born before this date is currently ongoing. Detailed statistical analysis can only be performed if all available data are included. However, based on the currently available information (185 patients), it may

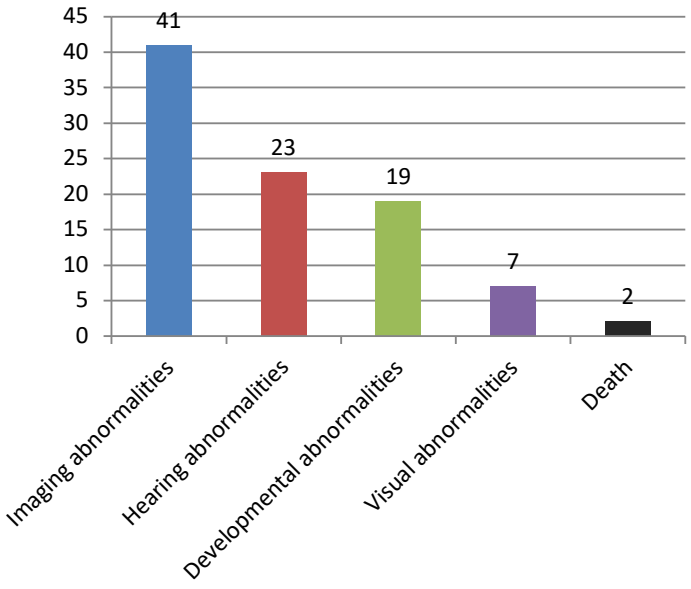
already be noted that since the start of the study in 2016, 50 children (27%) were asymptomatic at the time of the case report, while 135 had at least one complication. Of the symptomatic children, 62 (46%) received antiviral treatment. The complications observed in the newborns are shown in the following **chart:**

Chart 5 – Number of complications at the time of diagnosis, all children since the start of the study, n=185, (multiple answers possible)



One-year follow-up data are available for 113 patients, of whom 57 had clinical symptoms or signs (abnormalities detected in imaging, of hearing, development or vision), and 2 deaths occurred. All abnormalities detected by MRI, CT, ultrasound or EEG within a year after diagnosis of congenital CMV are classified as "imaging abnormalities". The status one year after birth is shown in the following **chart:**

Chart 6 – Anomalies detected 1 year after birth (multiple naming of symptoms per child are possible and will be counted individually).



Conclusions

No new recommendations for screening or the treatment of children with cCMV can yet be made on the basis of these preliminary results. The systematic recording of new cases in Switzerland and the one-year follow-up of all patients will provide a better understanding of the epidemiology and medium-term development of this disease.

Principal investigator

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4.3 Invasive Group A streptococcal (iGAS) infection

Background

GAS infections in children are typically mild and self-limiting, such as tonsillitis. In rare cases, they cause local suppurative complications and may occasionally lead to severe rheumatic complications (e.g. rheumatic fever). As perceived by members of the Pediatric Infectious Disease Group of Switzerland (PIGS), the frequency and severity of iGAS has increased in recent years. Several studies showed seasonal and regional differences in the incidence of iGAS, although local incidence remained relatively stable over time [1,2]. The reasons for this are largely unknown. One important risk factor for iGAS is primary varicella infection, but other types of skin damage such as excoriation or postoperative lesions have also been described as risk factors, as well as close contacts with GAS-infected patients [2]. Also important for the epidemiology of iGAS are the bacterial virulence factors or molecular characteristics such as the emm type [3].

To date, no epidemiological data are available on incidence, age distribution, clinical presentation or risk factors for iGAS in children in Switzerland. In addition, the molecular characteristics (pathogenicity factors) and emm types of the pathogenic GAS strains are largely unknown.

The survey of iGAS cases [4], which has been ongoing since December 1st, 2017, was planned for a study duration of four years. Due to the overall situation with the SARS-CoV-2 pandemic during the study period, coupled with the increased occurrence of respiratory transmitted diseases following the lifting of hygiene measures after the pandemic, the SPSU Committee approved the principal investigator's request to extend the study. In particular also because iGAS has been observed to have a seasonality parallel to that of respiratory infections and cases declined in 2020. A sharp increase in reported iGAS cases was evident during autumn / winter 2022 / 2023.

Aims of the study

Collection and analysis of data on iGAS in children in Switzerland aged ≤16 years with regard to:

- Incidence
- Seasonality
- Age distribution
- Clinical manifestations and complications
- Treatment
- Risk factors [underlying disease, varicella, drugs (e.g. ibuprofen, paracetamol)]
- Relapse rate
- Morbidity and mortality

Also planned is the collection of iGAS strains – initially only for storage, but subsequently also for emm typing in a separate project.

Case definition

Confirmed case

Isolation of Group A streptococci = GAS = Streptococcus pyogenes (by culture, antigen or PCR) from a normally sterile site such as:

- Blood
- Cerebrospinal fluid
- Puncture fluid (pleural, joint or pericardial fluid)
- Muscle / bone tissue (deep tissue, surgical specimen)

Probable case

Severe clinical presentation* with no alternative diagnosis AND isolation of GAS (by culture, antigen or PCR) from a non-sterile site

* Severe clinical presentation:

1 Toxic shock syndrome
Hypotension (systolic blood pressure <5th percentile for age)
PLUS ≥2 of the following criteria:

   a) Renal insufficiency (creatinine >2 x upper limit of normal range for age)
   b) Coagulopathy (platelet count <100 G/L or clinical signs of disseminated intravascular coagulation = DIC)
   c) Hepatic insufficiency (ALT, AST or bilirubin >2 x upper limit of normal range for age)
   d) Generalised rash with or without desquamation
   e) Acute respiratory distress syndrome (ARDS)

2 Necrotising fasciitis

Results

A total of 17 iGAS cases were reported in 2021. A total of 112 cases were reported in 2022, 79 (71%) of which were in the period from October to December. Detailed information on demographic and clinical characteristics, treatment, outcome and risk factors was obtained via questionnaires and was evaluated for all reported cases in 2021 and for 104 of the 112 reported cases in 2022. The children's median age was 55 months (4.5 years) in 2021 vs slightly higher in 2022 at 65 months (5.4 years) in 2022, with an age range of 11 months to 15 years (2021) vs 0 months to 16 years (2022). Gender distribution was similar in both years with 6 (35%) vs 38 (37%) female children, and 9 (53%) vs 61 (58%) male children in 2021 and 2022. Gender was unknown in 2 (12%) vs 5 (5%) of children. While cases were spread over the period from April to December in 2021, 79 (76%) of iGAS cases in 2022 were diagnosed in the period from October to December **(Chart 8)**. Information on disease severity with duration of hospital stay, ICU treatment, intubation, catecholamine requirements and surgical intervention as well as outcome are summarised in **Table 7**. With regard to the clinical presentation on admission in the reporting years 2021 and 2022, skin or soft tissue infection was reported in 3 children (18%) vs 42 (40%), osteoarticular infection in 2 (12%) vs 21 (20%), abscess in 7 (41%) vs 28 (27%), upper respiratory tract infection in 7 (41%) vs 34 (33%), pneumonia / pleural empyema in 5 (29%) vs 38 (37%), sepsis / bacteraemia in 3 (18%) vs 23 (22%), CNS infection in 0 vs 5 (5%) and toxic shock syndrome (TSS) in 0 vs 6 (6%). In 0 vs 16 (15%) of children, the iGAS infection occurred in connection with an acute varicella infection; in 0 vs 3 (3%) of cases, household contact with proof of GAS was reported. Underlying conditions were present in 2 (12%) vs 14 (14%) of children, with a variety of diagnoses (developmental delay, Hirschsprung's disease, hypothyroidism, diabetes mellitus, premature birth, bronchopulmonary dysplasia, asthma, haemato-oncological diagnosis, kidney transplant, Noonan syndrome, vascular malformation, oncological diagnosis, genetic disorder, autism).

Discussion and conclusions

Following very few Group A streptococcal infections in the two pandemic years 2020 (see SPSU Annual Report 2019 / 2020) and 2021, there was a sharp increase in cases in the fourth quarter of 2022. As in previous years, just under 90% of cases occurred in previously healthy children. Most recovered completely, but there were residual symptoms in 10% of all cases. In 2022 as before the pandemic, the most frequently observed risk factor was florid varicella infection, detected in fewer than 1 in 6 children with iGAS. While over half of patients required ICU treatment in 2021, only one third of children were treated in the ICU in 2022, despite total case numbers being almost five times higher. Intubation / ventilation was required in three times fewer cases, and three times fewer children needed circulatory support with catecholamines. One possible explanation for the lower proportion of severe cases in 2022 compared to previous years could be the relative increase in reports of skin and soft tissue infections with potentially less fulminant progression. Due to media attention following reports of rising iGAS case numbers in various European countries, e.g. in the UK [5], greater awareness among the reporting hospitals in Switzerland could also be a factor. Overall, despite considerably larger case numbers, there is currently no indication of greater Group A streptococci virulence; mortality fortunately remains low compared to other European countries at 1% [6,7]. To monitor the further course of iGAS epidemiology in Switzerland, the study duration for SPSU recording has been extended until November 30th, 2024.

Table 7 – Severity of the disease with duration of hospitalisation

Year	2021	2022
Average hospital stay in days (range)	14 (4 – 90)	10 (1 – 35)
Cases with ICU treatment	9 (53%)	34 (33%)
Duration of ICU treatment in days (range)	8.5 (2 – 32)	5.4 (1 – 26)
Intubation	5 (29%)	9 (9%)
Catecholamine requirements	6 (35%)	11 (11%)
Surgical treatment	8 (47%)	64 (62%)
Complete recovery	14 (82%)	83 (80%)
Recovery with residual symptoms	2 (12%)	15 (14%)
Deaths	0	1 (1%)
No information on residual symptoms at discharge	1 (6%)	5 (5%)

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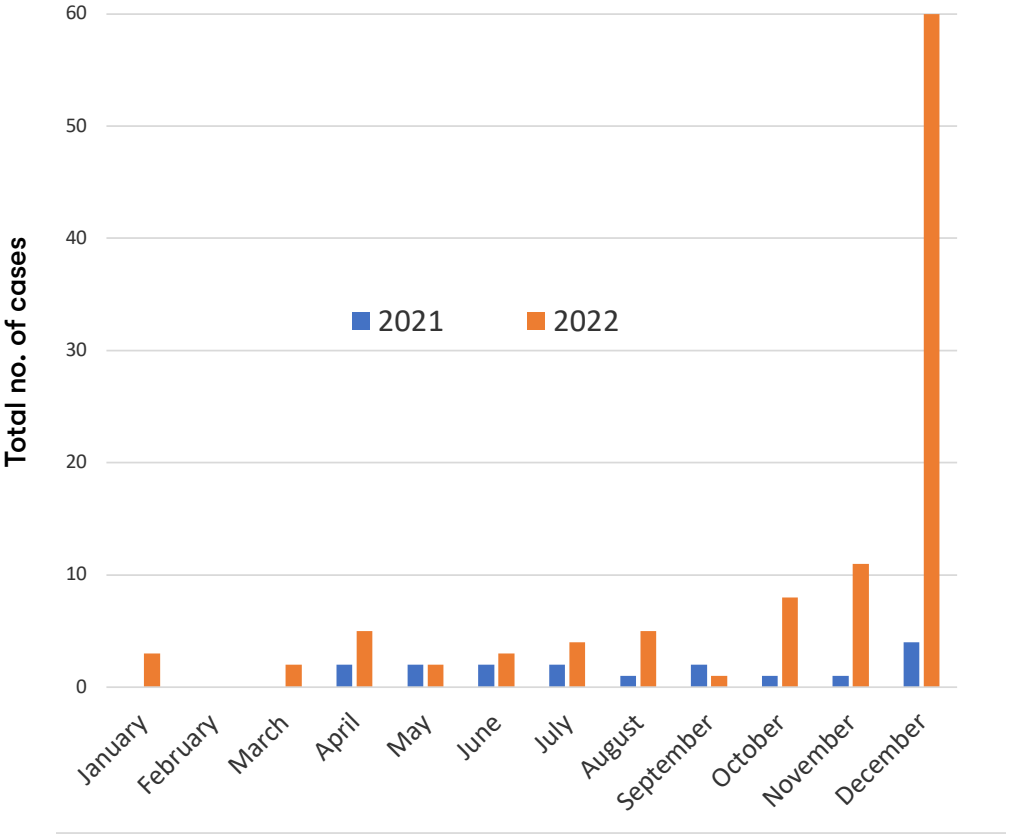
Chart 8


Total no. of cases
60
50
40
30
20
10
0
2021
2022
January
February
March
April
May
June
July
August
September
October
November
December

4.4 Vitamin K deficiency bleeding

Aims of the study

Various measures are available for the prevention of vitamin K deficiency bleeding (VKDB) [1,2]. In Switzerland, since 2003 [3], it has been recommended that newborns receive three oral doses of vitamin K (Konakion® MM, at 4 hours, 4 days and 4 weeks after birth) in order to prevent VKDB (official guidelines of paediatric switzerland). An earlier SPSU study showed that three oral doses of vitamin K offer adequate prophylaxis [4]. The most important current risk factors for VKDB are refusal of / failure to administer VK prophylaxis and undiagnosed hepatobiliary disease. The aim of this study is to determine the current epidemiology of VKDB, risk factors, and a possible increase or cluster effects, and thus to assess whether the prophylaxis recommended in 2003 remains appropriate in today's society.

Case definition

Bleeding in a newborn or infant aged ≤6 months (26 weeks):

- with an abnormal prothrombin time / Quick value <20% (international normalised ratio >4) in the presence of a normal (or increased) platelet count and normal fibrinogen (with no fibrin degradation products)
- with normalisation of prothrombin time / Quick value (and / or cessation of bleeding) within 30 – 120 minutes after administration of vitamin K.

Results

Between January 1st, 2021 and December 31st, 2022, 5 cases of VKDB were reported, of which only 3 cases met the case definition.

Conclusions

It is still too early to draw any conclusions concerning the incidence of VKDB since 2018. The study will continue as planned (2018 – 2024).

Principal investigator

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Table 9 – Overview of reports and cases 2018 – 2022

	No. of cases reported to SPSU	Total no. of cases	Confirmed cases	Not confirmed	Data unavailable / questionnaires not received
2019	3*	3	2	1	
2020	1	1	1	0	
2021	1	1	1	0	
2022	4	4	2	2	

*One report from November 2018 (study started on September 1st, 2018)

4.5 SARS-CoV-2 infection

Background

In late 2019, the first cases of coronavirus disease (COVID-19) were reported, which subsequently led to a rapid spread worldwide. On March 11th, 2020, the World Health Organization (WHO) declared the outbreak a pandemic. At that time models based on previous influenza pandemics, seasonal coronavirus prevalence, seasonal variation, and infection control efforts predicted multiple waves of COVID-19, with severe acute respiratory syndrome coronavirus (SARS-CoV-2) eventually becoming a seasonal virus. Current models and forecasts including data from three years of the pandemic and after evolution of several virus variants and vaccine introduction are prudent. One important and unpredictable factor will be the emergence of new variants and how these may look like.

The large number of individuals worldwide who have been infected with the disease, including children, has resulted in the accumulation of knowledge regarding its spread, clinical manifestations, and optimal management approaches. Ongoing surveillance will continue to be important, even as our understanding of the infection and resulting disease has improved. It will be particularly important to monitor new variants, the potential for waning immunity, and the effects on new birth cohorts. Lastly, ongoing surveillance will also help us understand the effectiveness of vaccines and other public health interventions, and guide future decision-making about disease control measures.

Aim of the study

The aim of the study is to collect epidemiological data on SARS-CoV-2 infections and PIMS-TS in children in Switzerland, so as to determine the following:

- Demographic characteristics (age, sex, co-morbidities, etc.)
- Incidence (age-stratified)
- Clinical disease spectrum and disease severity incl. cases of PIMS-TS
- Mortality (age-stratified)
- Co-morbidity and risk factors for severe disease
- Intensive care and respiratory support
- Therapeutic approaches
- Course of disease
- Transmission patterns
- Changes in epidemiology and clinical presentation with the emerge of new variants of concern (VOC)
- The effect of vaccination on the above points

Case definition

Children aged <18 years treated in a Swiss hospital for COVID-19 and / or PIMS-TS confirmed by one of the tests specified below:

- Detection of SARS-CoV-2 in a clinical specimen by a validated nucleic acid amplification test (PCR), serology or rapid antigen test.
- Diagnosis of PIMS-TS in accordance with the Swiss national recommendations (Schlapbach et al. Front. Pediatr., 26 May 2021; doi.org/10.3389/fped.2021.667507)

Changes occurring during the study period

From March 1st to October 31st, 2020, both outpatient and hospitalised cases were reported.

From November 1st, 2020, only hospitalised cases were reported, but specifically also cases of PIMS-TS. PIMS-TS cases reported before November 1st, 2020 were retrospectively identified. For all reported PIMS-TS cases, a follow-up questionnaire for data collection purposes was sent out 4 to 6 weeks after discharge.

In June 2022, the questionnaire was shortened to make the participation more feasible, given the large number of COVID-19 cases admitted during the delta wave and to adjust it to the current state of research.

Results

Study population

From January 1st, 2021 to December 31st, 2022 a detailed dataset was returned for 1218 cases, of which 1201 were included in the final analysis (17 duplicates were removed). The age of the children ranged from 1 day to 17.8 years (median 1.2, interquartile range (IQR) 0.2 – 7.3 years) **(Table 10)**.

Ethnicity of the children admitted to hospital were Caucasian (n=810 [67.4%]), Black (n=47 [3.9%|), Arabic (n=43 [3.6%]), Hispanic (n=23 [1.9%]), Asian (n=17 [1.4%]), and unknown (n=96 [8.0%]).

Admission to ICU and management

A total of 140 (11.6%) children required ICU admission for the following reasons: hemodynamic instability (n=27 [19.2%]), respiratory failure (n=40 [28.6%]), and other reasons (n=71 [50.7%]). Among the hospitalised cases, 221 (18.4%) required oxygen, 43 (3.6%) inotropes and 25 (2.1%) cases had mechanical ventilation. Most of the children (920 [76.6%]) did not receive any medication during their hospitalisation. However, among all hospitalised children, 204 (17.0%) received corticosteroids, 106 (8.8%) received intravenous immunoglobulins. Among ICU-admitted children, 84 (60%) received corticosteroids and 56 (40%) were treated with intravenous immuno-globulins. The median duration of hospitalisation for non-ICU admitted children was 2.0 (IQR 1.0 – 4.0) days and for children admitted to ICU 7 (IQR 5.0 – 11.25) days.

Symptoms

Overall, fever was the most common symptom observed in children with SARS-CoV-2 infection (847 [70.5%]), followed by rhinorrhea (477 [39.7%]) and cough (451 [37.6%]) **(Table 10)**. Seizure, conjunctivitis, and headache were added to the modified questionnaire in the summer of 2022 and have since been observed in 21 (1.7%), 5 (0.4%), and 2 (0.2%) children, respectively. Among the 140 children admitted to the ICU, fever was the most frequent symptom (110 [78.6%]). Other common symptoms included oxygen saturation <92% (55 [45.8%]), respiratory distress (63 [45.0%]), vomiting (61 [43.6%]), and abdominal pain (55 [39.2%]).

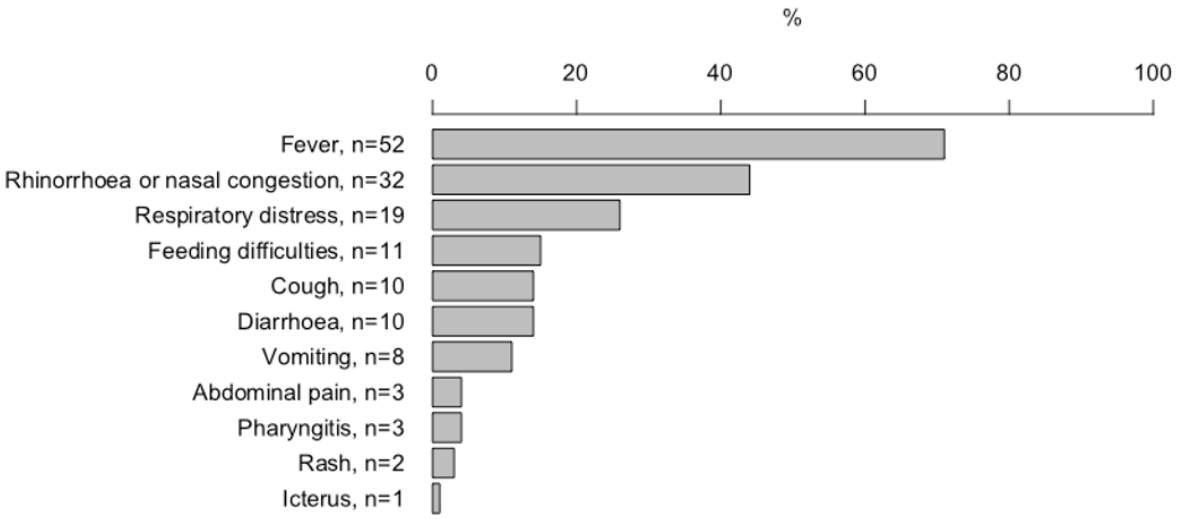
Table 10 –Baseline characteristics of children admitted with SARS-CoV-2

	All hospitalised n (%) n=1201	ICU n (%) n=140
Age		
<1 month	153 (12.7)	12 (8.5)
>1 month to <2 years	364 (30.3)	27 (19.3)
2 to <5 years	124 (10.3)	18 (12.9)
5 to <10 years	175 (14.5)	36 (25.7)
≥10 Jahre	200 (16.7)	46 (32.9)
Missing	185 (15.4)	1 (0.7)
Female	538 (44.8)	54 (38.6)
Comorbidities	113 (9.4)	26 (18.6)
Symptoms		
Fever	847 (70.5)	110 (78.6)
Cough	451 (37.6)	39 (27.9)
Rhinorrhoea	477 (39.7)	36 (25.7)
Pharyngitis	238 (19.8)	29 (20.7)
Anosmia / dysgeusia	10 (0.8)	0 (0.0)
Abdominal pain	209 (17.4)	55 (39.2)
Diarrhoea	190 (15.8)	36 (25.7)
Vomiting	259 (21.6)	61 (43.6)
Respiratory distress	287 (23.9)	63 (45.0)
Rash	133 (11.1)	44 (36.7)
Oxygen saturation <92%	190 (15.8)	55 (45.8)
Seizure	21 (1.7)	5 (3.6)
Conjunctivitis	5 (0.4)	1 (0.7)
Headache	2 (0.2)	1 (0.7)

Neonates

Neonates were analysed separately for the period between March 1st, 2020, and September 30th, 2021. The analysis included 73 neo-nates, of which 7 (10%) were born preterm. The median age at admission was 17 days (interquartile range [IQR] 11 – 23), and 40 (55%) of the neonates were female. Most of the neonates (64 [88%]) were admitted from their homes. The most common symptom observed among neonates was fever (52 [71%]), followed by rhinorrhoea / nasal congestion (32 [44%]) and respiratory distress (19 [26%]) **(Chart 11).** Twenty (27%) neonates presented with fever without any apparent source. Seven (10%) neonates were transferred to the intensive care unit, and one (1%) neonate required inotropic support. All neonates for whom data were available were discharged to their homes without any persisting symptoms.

Chart 11 – Distribution of symptoms in neonates with SARS-CoV-2 infection



Comorbidities and co-infections

A total of 113 (9.4%) children had pre-existing medical conditions. The most common comorbidities were reported in the following groups: respiratory (46 [40.7%]), cardiovascular (28 [24.8%]), and haemato-oncological (31 [27.4%]). Among the children admitted to the ICU, 26 (18.6%) had pre-existing comorbidities: 16 (11.4%) had respiratory, 5 (3.5%) had cardiovascular, and 2 (1.4%) had haemato-oncological comorbidities. Two (1.4%) children had previously been diagnosed with type 1 diabetes mellitus.

Among all hospitalised children, in 71 (5.9%) RSV was detected in the nasopharyngeal swab, Influenza was detected in 12 (1.0%) and other viruses such as Rhino- / Enterovirus, Picornavirus and Adenovirus were detected in 68 (5.7%). When only considering children admitted to the ICU, 8 (5.7%) had RSV, 1 (0.7%) had Influenza, and 7 (5.0%) had other viruses detected in their nasopharyngeal swab.

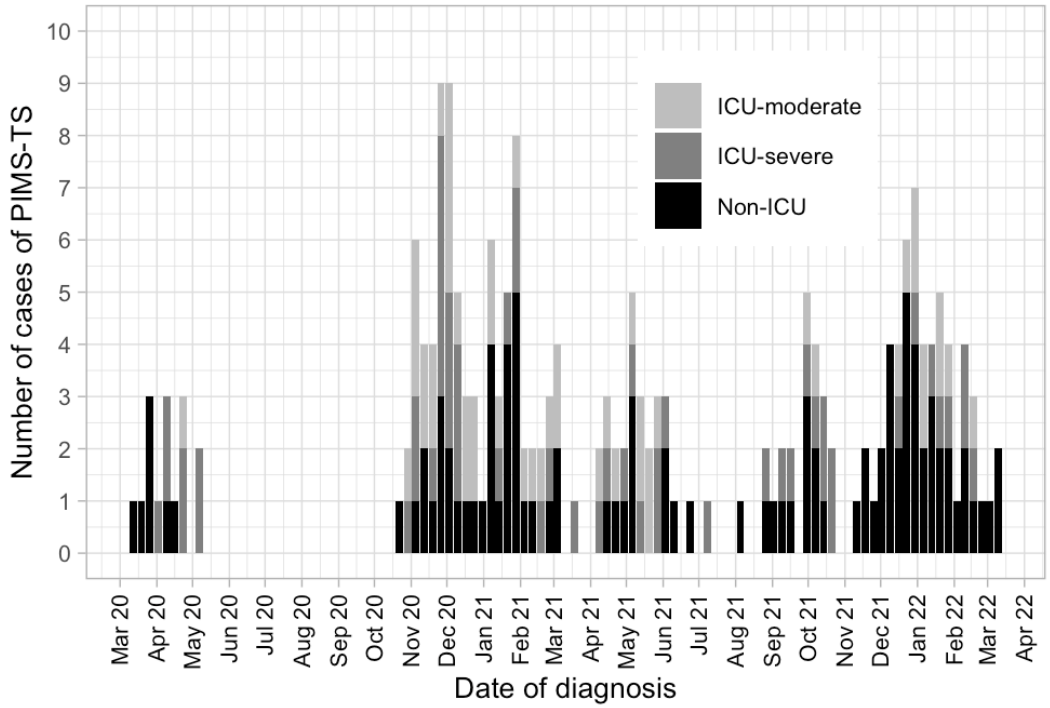
PIMS-TS

An independent analysis including children hospitalised with PIMS-TS between March 2020 and March 2022, identified 204 children. The median age of the children was 9.0 years (interquartile range (IQR) 6.0 to 11.5), and 142 (69.6%) of them were male. **Chart 12** shows the trend of reported PIMS-TS cases over time.

More than half of the children (105/204 [51.5%]) required ICU admission, and 55 (52.4%) of them inotropic support. Among these, 14 (13.3%) also required mechanical ventilation. Echocardiography was performed for 201 (98.5%) of the children, and among them, 132 (64.7%) showed cardiac abnormalities such as left ventricular systolic dysfunction (73 [36.3%]), coronary artery abnormality (45 [22.4%]), and pericardial effusion (50 [24.9%]).

A follow-up was done four to six weeks after hospital discharge. Data from follow-up was available for 194 (95.1%) children. While none of the children had left ventricular systolic dysfunction during follow-up, 12 (6.6%) and 3 (1.7%) children still showed coronary abnormality and pericardial effusion, respectively. At follow-up, 15 (7.9%) reported a limitation in daily life activity because of fatigue and 16 (8.9%) children had impaired school or kindergarten attendance. Children who had been admitted to ICU had a higher rate of impaired school / kindergarten attendance compared to those who had not.

Chart 12 – Number of PIMS-TS cases admitted over time from March 2020 to March 2022



Complications

In 2021 and 2022, complications were reported in 115 (9.6%) of the hospitalised children. The most frequent complications were cardiovascular (25 [2.1%]), bacterial co- / superinfection (21 [1.7%]), followed by neurological (17 [1.4%]) and respiratory complications (9 [0.74%]). Two deaths were recorded (0.16%).

Vaccination

Most children (755 [62.8%]) had not received a COVID-19 vaccine. 3 (0.2%) children had received one dose, 8 (0.7%) had received two or more doses. The COVID-19 vaccination status was unknown for 147 (12.2%) children. None the children admitted to ICU were vaccinated.

Conclusions

COVID-19 is mostly a mild disease in children and adolescents with low mortality. The clinical spectrum and severity are influenced by age in paediatric COVID-19. Neonates have mainly a mild spectrum of disease with fever but are commonly hospitalised for evaluation of bacterial infection. PIMS-TS a severe delayed manifestation of COVID-19 infection. Longer-term follow up however shows restitution of cardiac function but coronary artery changes may remain longer. Continuous observation is necessary to further understand paediatric COVID-19, guide therapy and evaluate the necessity for vaccination in children.

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4.6 Varicella-zoster-virus associated hospitalisations (Including post-infectious complications)

Background

Many believe that varicella, a common infectious disease, is a benign childhood disease. This may be true for most cases, however there are noteworthy and serious exceptions [1]. In Switzerland VZV associated hospitalisations were previously reported to SPSU from 2000 to 2003. During these years, a total of 335 cases were identified. The mean age of patients was 4.1 years (median 3.5 years, range 0 – 16 years). Of these, 13% were immunocompromised. Most common complications in both immunocompetent and immunosuppressed patients were secondary bacterial infections and central nervous system involvement. 3% required intensive care and three died. The calculated hospitalisation rate was 13 per 104 cases [2]. In Switzerland age-specific seroprevalence in children <5 years is 37% and by 15 years this reaches about 96% [3]. About 5% of children and adolescents escape VZV infection (especially those who grow up without siblings) and, in the absence of immunisation, remain susceptible [4] and thereby enter an age-group (adulthood) at much higher risk of severe complications [5,6]. When this surveillance started, the vaccination strategy in Switzerland recommended that, due to the elevated risk of complications in adults, VZV infection should be prevented in anyone up to 40 years of age who did not have chickenpox as a child. Vaccination against chickenpox (varicella) is therefore recommended for all adolescents between 11 and 15 years of age who are not immune (catch-up vaccination for adults up to the age of 39) [7]. During a monitoring period (2014 – 2016) of VZV vaccination up-take, the Swiss Federal Office of Public Health noted that only 1% of adolescents at 16 years had received 2 doses of vaccine [8]. As of January 2023, a universal varicella immunization program has been introduced in Switzerland (www.bag.admin.ch/impfplan). The results of a recent publication on surveillance data of VZV complications in England, a country where universal VZV vaccination has not been implemented but is under discussion, show that the hospitalization and complication incidence has increased by 25% and 24% respectively, when comparing the years 2004 to 2017 [11]. VZV hospitalizations and complications have decreased dramatically in the USA [9] and Germany [10] after implementation of a universal VZV vaccination strategy.

Data from VZV hospitalisation surveillance programs which were implemented in Australia and New Zealand in the past (www.inopsu.com) delivered evidence to support the implementation of national VZV vaccination programs. In Switzerland recent data on varicella associated hospitalizations and complications are missing. However, these are necessary as they will give a portrait of children hospitalized for varicella, reflecting what could be prevented by vaccination. With the recent introduction of universal VZV vaccination in Switzerland, this project will help to estimate its effect by demonstrating a reduction of hospitalized cases when compared to the preimmunization period.

Aims of the surveillance

Surveillance of type and frequency of VZV associated complications leading to hospitalization in Switzerland to review the epidemiology, risk factors, exposures, VZV vaccination, complications, clinical management, antibiotic exposure, hospital days (incl. ICU) and outcome during the implemented prevention strategies. Comparison with previous SPSU VZV surveillance data and international data.

Methods

Observational, multicentric surveillance with reporting of all children and adolescents ≤ 16 years of age hospitalized in one of the SPSU participating hospitals with VZV infections, i.e. varicella, herpes zoster or post infectious complications (eg. stroke). Reporters will be encouraged to report VZV associated ischemic stroke also to the Swiss Neuropediatric Stroke Registry (https://snpsr.neuropaediatrie.ch/) and vice versa we will be informed about cases reported to the Swiss Neuropediatric Stroke Registry during the study period. After notification to SPSU by participating hospitals / clinics an anonymized CRF (fillable pdf) is linked to the notifying centre for data entry and returned.

Reporting criteria and case definition

All children < 16 years with clinical manifestations of VZV infection (ICD-10: B01.-) leading to hospitalization.

Results

Ten and 81 fully completed case report forms were returned in 2021 (starting July 1st) and in 2022 to the study center respectively. The predominant age group affected with VZV associated manifestations were immunocompetent children 1 to 9 years with a male predominance. Most VZV exposure was outside the family and no infected cases were previously vaccinated against VZV **(Table 13)**. Looking at manifestations three and seven zoster cases were reported in 2021 and 2022 respectively. Most (>71%) of these occurred in the immunocompromised and in the adolescent age group. No cases of congenital VZV and one case of VZV associated stroke (2.5-year-old female) were reported. The largest group included primary varicella infections: 7 (2021) and 73 (2022). Mean hospitalization duration was 6.5 (2021) and 8 (2022) days. An increase in VZV associated hospitalization was observed in 2022 peaking in December **(Chart 15)**.

In 16% of reported cases, management on intensive care was necessary and 16% of cases at least one surgical intervention was necessary. Two deaths (invasive bacterial infections with fulminant sepsis and multi-organ failure) with concurrent VZV infection were reported: 1 case (4-year-old male) with Streptococcus pyogenes and 1 case (5-year-old-female) with Streptococcus pneumoniae infections. Both were immunocompetent, unvaccinated and without chronic illnesses. Most of the reported complications **(Table 14)** in children hospitalized with VZV were secondary bacterial infections of the skin, soft-tissue, and muscle. No concurrent invasive Group A strepto-coccal (S.pyogenes) infections were reported in 2021, however 18 of the 79 primary VZV cases were affected in 2022, most occurred during the second half of that year.

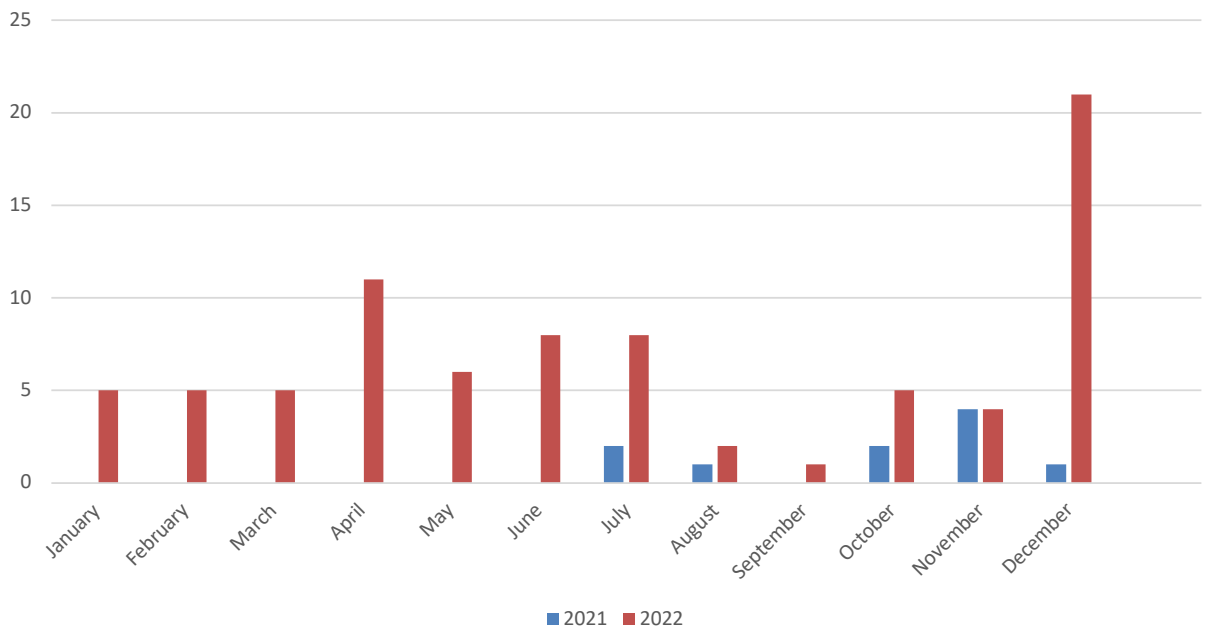
Table 13 – Characteristics of the 2021* – 2022 reported VZV hospitalization cases (* surveillance started July 1st, 2021).

			2021* N (%)	2022 N (%)
Case reports		Total	10	81
Manifestation	Primary VZV		7 (70)	73 (90)
	Zoster		3 (30)	7 (9)
	Stroke(post infectious complications)		0 (0)	1 (1)
	Congenital VZV		0 (0)	0 (0)
Sex	Female		5 (50)	30 (37)
	Male		5 (50)	51 (63)
Age at admission	<1 y		4 (40)	11 (14)
	1 – 4 y		2 (20)	46 (57)
	5 – 9 y		2 (20)	18 (22)
	10 – 16 y		2 (20)	6 (7)
VZV Exposure	within family		3 (30)	27 (33)
	outside family		7 (70)	54 (67)
VZV vaccinated	yes		0 (0)	0 (0)
	no		10 (100)	69 (85)
	unknown		0 (0)	12 (15)
Immunocompromised (primary or secondary)			4 (40)	9 (11)
Intensive care			1 (10)	15 (16)
Surgical intervention (cases)			0 (0)	13 (16)
Hospitalisation duration (d): mean(range)			6.5 (1 – 16)	8 (1 – 20)
Deaths			0 (0)	2 (2.5)
Immuocompromised			0 (0)	0 (0)

Table 14 – Main complications of the 2021* – 2022 reported VZV hospitalization cases (* surveillance started July 1st, 2021). Some cases had multiple complications.

Main complications		2021* N	2022 N
Secondary bacterial infections			
	Skin / soft-tissue / abscess		32
	Necrotizing fasciitis		6
	Purpura fulminans		1
	Lymphadenitis		1
	Bacterial pneumonia		9
	Osteoarticular infection		1
	Sepsis		2
	invasive GAS infection		18
CNS related VZV complication			
	Encephalitis		2
	Cerebellitis		6
	Meningitis		2

Chart 15 – VZV hospitalisations (cases per month) from 2021* to 2022 (*surveillance started July 1st, 2021).



Discussion

Although the surveillance was started in July 2021, a steep increase of VZV hospitalisations can be observed in 2022, dramatically peaking in December. An increase in infection-related hospitalisations from 2022 was also observed and reported with other pathogens (eg. RSV) in Switzerland and Europe [12,13]. Reasons for this may be related to the lifted COVID-19 precaution measures in 2021 and increased contact opportunities within the population from 2022. In the previous SPSU surveillance (2000 – 2003) case numbers of 60 to 80 per year were also reported [2]. The age-group most affected were the 1- to 4-year-old children as observed in this cohort. The amount (18 cases in 73 VZV hospitalisations) of concurrent invasive Group A Streptococcal (iGAS) infections during a period of 12 months is impressive. In the former cohort this was observed in 21 cases however over a period of 3 years. See summary and discussion in the SPSU iGAS report. It is known that VZV is a predisposing risk factor for secondary bacterial infections, particularly iGAS. The described cohort of the past 18 months is a population without the implementation of a universal varicella immunization. The SPSU surveillance of VZV hospitalisations will continue through June 2026. It will be interesting to see how the epidemiology will change, since universal varicella immunization was introduced in Switzerland in January 2023.

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4.7 Acute paediatric hepatitis of unknown origin

Background

Most cases of acute hepatitis in children are mild and transient, and those of clinical significance are usually due to hepatitis viruses A-to-E. Since early 2022, an unusually high number of acute hepatitis of unknown origin have been reported, mainly in the United Kingdom [1], but also in the USA, France, Belgium, Spain, Italy, Norway, Romania, the Netherlands, New Zealand and Denmark [2]. As of May 6th, 2022, several cases in Switzerland met the WHO case definition [3]. This syndrome mostly affects previously healthy children aged 2 – 5 years but cases up to 16 years have been described [1,2]. The most frequently reported symptoms are jaundice, vomiting, abdominal pain, pale stool, diarrhea, lethargy, and malaise [1,2,4,5]. The reported frequency of fever varies between 0% to 55% [1,2,4,6]. Between 7% to 10% of documented cases have required liver transplantation [2,7]. Despite an extensive infectious, immunological and toxicological workup, the etiology of this entity remains unclear. There is no clear association with travel or recent vaccination. Adenovirus has been identified in about 60 – 70% of cases, either in blood, upper respiratory tract or stools. The most frequently identified adenovirus is adenovirus type 41 [2,4,7]. However, it is not clear whether this simply reflects sustained circulation of adeno-viruses in the pediatric community. Moreover, low viral load in blood [2,4] and negative PCR on explant biopsies (personal communication) children having undergone liver transplant do not support the hypothesis of a primary adenovirus hepatitis. Similarly, SARS-CoV-2 has also be identified in some cases, but it could simply reflect community circulation. For example, out of the 114 cases reported in the UK, 60 (53%) were positive for adenovirus and 18 (16%) for SARS-CoV-2 [2]. Other working hypotheses include a new viral variant of adenovirus or SARS-CoV-2, a coinfection, an immune-mediated hepatitis triggered by a viral infection in a relatively naïve pediatric population or a toxic agent.

Aims of the Study

We aim to rapidly implement a nationwide surveillance system for acute non-A-to-E hepatitis in children n <16 years with the following aims:

Primary aim

- Identify the epidemiology of acute non A-to-E hepatitis

Secondary aims

- Identify the etiology of acute non A-to-E hepatitis
- Characterize the clinical presentation of acute non A-to-E hepatitis
- Identify risk factors for occurrence of acute non A-to-E hepatitis
- Analyze risk factors for a severe course (liver failure and liver transplantation)
- Analyze management of acute non A-to-E hepatitis with a view to streamline and rationalize management

Duration of the study:
July 1st, 2023 – June 30th, 2027

Case definition

In order to allow for international comparisons, we will follow the World Health Organisation (WHO) accepted case definition [3]:

- Confirmed: N/A
- Probable: A person presenting with an acute hepatitis (non-hepatitis viruses A, B, C, D and E*) with aspartate transaminase (AST) or alanine transaminase (ALT) over 500 IU/L, who is 16 years old or younger, since October 1st, 2021.

Results

Four of the 6 (4/6) cases reported were notified as having occurred between March 1st, 2022 – June, 30th, 2022.

Conclusion

Primary aim:

In Switzerland there were 2 cases of acute hepatitis during the study period, and 4 in the period overlapping with the other reported cases in Europe ie before the initiation of the SPSU study. Although the forms were not forwarded to the PI in time for this report, it is important to emphasize that none warranted liver transplantation. This information steams from the fact that the PIs work in the only pediatric liver transplantation center in the country. In summary, acute non- A–E hepatitis was not a clinical or public health problem in Switzerland since the study initiation.

Secondary aims:

Given the low numbers of cases and the lack of reporting, no conclusions can be drawn regarding the secondary aims.

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