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CASE STUDY

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Influenza vaccine uptake in juvenile idiopathic arthritis during the COVID-19 pandemic: a multi-centre cross-sectional study by PRES vaccination working party

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Abstract

Background Children with rheumatic diseases are at risk for contracting severe influenza and COVID-19 and are thus targeted for these vaccination.

Objectives To assess the influenza (flu) vaccination rate in children with Juvenile Idiopathic Arthritis (JIA), investigate families' attitudes towards the influenza vaccine, and the effect of the COVID-19 pandemic on flu vaccine uptake.

Methods This multi-centre, cross-sectional study was conducted across 9 countries. JIA caregivers completed an anonymous questionnaire about their children's influenza vaccination, including the 2019–2020 and 2020–2021 seasons, including knowledge, and perceptions regarding influenza vaccination.

Results Based on responses from 655 JIA caregivers, 152 children (23.2%) received influenza vaccinations in the 2020–2021 season, representing a significant rise from 18.6% in the previous season ($p < 0.01$). The likelihood of vaccination was higher among employed/self-employed caregivers compared to unemployed (28.2% and 29.9% vs. 13.9%), and those with tertiary education versus elementary (28% vs. 9.7%), both $p < 0.01$. Concerns of children's vulnerability to SARS-CoV-2 and severe COVID-19 disease due to JIA were prevalent (51.3% and 85.3% respectively), with 51.3% supporting COVID-19 vaccination. Caregivers who previously vaccinated their children for influenza showed a greater inclination towards SARS-CoV-2 vaccination (73.4% and 79.5%, $p < 0.01$).

Conclusions Families of children with JIA reported an increasing flu vaccine uptake and a high intention for COVID-19 vaccine administration. Previous vaccination behavior was shown as a significant predictor of future behaviour. Strengthening health education may address fears and lead to better vaccine coverage against both influenza and SARS-CoV-2 in children with JIA and other inflammatory rheumatic diseases.

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Keywords Influenza vaccine, Juvenile Idiopathic Arthritis (JIA), COVID-19, Vaccination, Children

Introduction

Every year, the influenza virus spreads globally, with significant pediatric and adult infection rates [1]. Influenza is a major public health problem, increasing hospitalisations, morbidity and mortality, worldwide [2, 3]. Numerous medical conditions, including inflammatory rheumatic diseases (IRDs), increase an individual's risk of acquiring influenza or developing serious complications [4]. Children with IRDs are more vulnerable to infections such as influenza compared to healthy individuals due to the disease itself and to treatment with immunomodulating drugs [5].

Seasonal influenza (flu) vaccination is the most effective approach to prevent infection and reduce mortality [6]. Annual vaccination is an important intervention to protect children with Juvenile Idiopathic Arthritis (JIA) against influenza. Despite recommendations from the European League Against Rheumatism (EULAR) for annual influenza vaccination in patients with paediatric IRDs [7, 8] and numerous studies proving its safety and efficacy [9], adherence to vaccination guidelines and influenza vaccine uptake in this group remain unknown.

Since the onset of the COVID-19 pandemic, children have been susceptible to both influenza and COVID-19 and may be co-infected and transmit both respiratory viruses to others [10]. In general, children represent a small proportion of severe COVID-19 cases or deaths, as they are mostly mildly or even asymptomatically affected by the SARS-CoV-2 virus [11, 12]. Unlikeadults with chronic conditions, children with IRDs do not appear at higher risk of severe COVID-19 disease [13, 14]. A full understanding of their immune response to this specific virus is still lacking. Immune dysregulation contributes to severe COVID-19 disease and it also appears to explain the multisystem inflammatory syndrome (MIS-C) reported in children [10, 12]. This hyperinflammatory syndrome in children with IRDs can be severe and mimic their underlying illness [13]. Thus, COVID-19 vaccines for children are required for direct and community protection [15] and to prevent MIS-C [16]. Although COVID-19 vaccine hesitancy among adults is well studied [17, 18], little is known about parental hesitancy for COVID-19 vaccines for children [19, 20].

The COVID-19 pandemic increased uptake of protective behaviours, including handwashing and social distancing [21, 22]. Therefore, the pandemic may have also encouraged vaccination behaviour, but this remains unknown. Several studies demonstrated a partial cross-protection from flu vaccination [23, 24]. In this context, at the beginning of the 2020–2021 cold season, vaccination against the flu represented one of the most effective strategies to attenuate the impacts of the influenza virus and the COVID-19 pandemic [23, 24].

Attitudes toward COVID-19 vaccinations have been investigated among the general population. However, studies investigating caregivers' knowledge and attitudes toward both the influenza and COVID-19 vaccinations in the paediatric population and especially in children with IRDs are lacking [13].

This collaborative, multi-centred descriptive study aimed to identify families' views and attitudes towards influenza and COVID-19 vaccination considering the SARS-CoV-2 pandemic; to assess the influenza vaccination rate in children with JIA, and investigate caregivers' knowledge, perceptions, and practices about influenza vaccine uptake, aiming to identify barriers and facilitators that may improve the vaccination services offered to young patients with IRDs. The study also explored families' perceptions of COVID-19 in JIA patients and their intention to vaccinate against it, as well as evaluating how the pandemic influenced parents' intention to have their children receive the influenza vaccine.

Methods

This multi-centre cross-sectional study was conducted by the Vaccination Working Party of Pediatric Rheumatology European Society (PReS) using a voluntary, anonymous questionnaire distributed to caregivers of children with JIA across 9 countries. The paper questionnaire was provided in the native language in each participating country during the clinic visit. Questionnaires included influenza vaccine history, including the year of 2020–2021, COVID-19 vaccine intentions, and social, demographic, and clinical data.

Statistics

Descriptive statistics calculated absolute and relative frequencies. Associations were evaluated using the Chi-square test of independence to determine the significant factors associated with caregivers' perceptions regarding the flu and COVID-19 vaccines. The significance level was set at $p \leq 0.05$. Analysis was performed using SPSS v.20.

Results

A total of 655 JIA caregivers (73.1% female) across 9 countries participated (Tables 1 and 2). Most were employed (61.2%), married (78.5%) and 43.1% had a tertiary-level education. Median patient age was 11 years (IQR: 7–15) with a median disease duration of 3.5 years (IQR: 2–6.5; Table 2). The major diagnosis was oligoarticular JIA (34%), followed by poly-articular JIA (22%),

Table 1 Influenza vaccine uptake among countries in 2019–2020 and 2020–2021 seasons and intention of COVID-19 vaccine administration in the future in the 2020–2021 season

Country	Participants *N* (%)	Flu vaccine uptake in 2019–2020 season *N* (%)	Flu vaccine uptake in 2020–2021 season *N* (%)	Intention of COVID-19 vaccine administration *N* (%)
Croatia	76 (11.6)	20 (26.3)	21 (27.6)	38 (50)
Greece	29 (4.5)	23 (79.3)	29 (100)	21 (72.4)
Israel	74 (11.3)	35 (47.3)	37 (50)	47 (63.5)
Italy	14 (2.1)	2 (14.3)	6 (42.9)	11 (78.6)
Poland	48 (7.3)	14 (29.2)	10 (20.8)	36 (75)
Russia	66 (10.1)	6 (9.1)	5 (7.4)	11 (16.7)
Slovakia	73 (11.1)	3 (4.1)	24 (32.9)	40 (54.8)
Slovenia	85 (13)	8 (9.4)	24 (28.2)	29 (34.1)
Turkey	190 (29)	11 (5.8)	2 (1.1)	103 (54.2)
Total	655	122 (18.6)	158 (24.1)	336 (51.3)

Table 2 Baseline demographics and clinical characteristics of JIA patients

Variable	N (%)
Median Age, years	11 (IQR: 7–15)
Female sex	478 (73.1%)
Median disease duration, years	3.5 (IQR: 2-6.5)
Disease classification (*N* = 655)	
Oligo-articular JIA	223 (34%)
Poly-articular JIA	144 (22%)
Enthesitis-related arthritis	84 (12.8%)
Psoriatic JIA	33 (5%)
Systemic JIA	82 (12.5%)
Undifferentiated	28 (4.2%)
Do not know	61 (9.4%)
Participating Countries	
Turkey	190 (29%)
Slovenia	85 (13%)
Croatia	76 (11.6%)
Israel	74 (11.3%)
Slovakia	73 (11.1%)
Russia	66 (10.1%)
Poland	48 (7.3%)
Greece	29 (4.5%)
Italy	14 (2.1%)
Current treatment	
Methotrexate	324 (49.5%)
Anti-Tumor Necrosis Factor-α	199 (30.4%)
Corticosteroids	48 (7.3%)
Anti-interleukin 6	43 (6.6%)
Anti-interleukin 1	29 (4.4%)
Abatacept	4 (0.6%)

JIA, Juvenile idiopathic arthritis

enthesitis-related arthritis (ERA) (12.8%), systemic JIA (12.5%) and psoriatic JIA (5%) (Table 2). Most patients were treated systemically (81%); commonly with methotrexate (49.5%) and anti-TNFa (30.4%) (Table 2).

Influenza vaccination findings

85% of caregivers reported that their child was vaccinated according to their national vaccination schedules. However, only 21.7% had ever received an influenza vaccine. A total of 122 (18.6%) were vaccinated against influenza in the 2019–2020 season and 158 children (24.1%) were vaccinated in the 2020–2021 season. In 2021, 87.3% were in a stable disease state at the time of the immunisation.

In the 2021 season, most of the caregivers received recommendation for flu vaccination by their paediatric rheumatologist (33.5%) and/or paediatrician (25%).

Caregivers who were employed or self-employed caregivers showed a higher flu vaccination for their children, with 28.2% and 29.9% respectively, compared to those who were unemployed (13.6%). Similarly, caregivers with a tertiary education had a higher vaccination rate (28%) compared to those with only an elementary level education (9.7%); both comparisons demonstrating significant differences ($p < 0.01$). Children with psoriatic JIA and poly-articular JIA had the highest vaccine uptake (both 30%), while patients with undifferentiated JIA reported the lowest (7.4%; $p < 0.01$).

Among flu vaccinators in the 2020–2021 season, 92.4% had been vaccinated according to national vaccination schedules, 64.6% had been immunized against influenza in previous years, while 57.6% received the flu vaccine during the 2019–2020 season ($p < 0.05$). A significant increase was reported for influenza vaccine uptake between 2019 and 2020 and 2020–2021 seasons (18.6% vs. 24.1%, $p < 0.01$).

Caregivers who were informed of influenza vaccine recommendations by medical staff were more likely to vaccinate their children against flu in the current season (43.5%, $p < 0.01$). However, among non-vaccinators, 52% did not have the chance to discuss their concerns with a specialist. Major reasons for non-vaccination included lack of knowledge regarding the need (36%) and fear of side-effects (24.5%); 12.5% reported the vaccine was

unavailable. Personal beliefs drove non-vaccination in 41.5% of cases, while 13% reported it was their doctor's advice. Caregivers suggested that informing families in advance (67%) may improve flu vaccine uptake in the future.

COVID-19 vaccination findings

A high proportion of caregivers expressed concerns regarding their child's vulnerability to SARS-CoV-2 due to JIA (51.3%), as well as their risk of severe COVID-19 disease (85.3%). Therefore, 51.3% were in favour of their child receiving the COVID-19 vaccine (Table 1). Caregivers worried about their children becoming infected by SARS-CoV-2 and facing serious disease were far more likely to vaccinate them against SARS-CoV-2 (55.6% versus 26.2%, $p < 0.01$). Variations were also reported based on the child's diagnosis. Children with psoriatic JIA and ERA were more likely to obtain COVID-19 vaccine compared to children with systemic JIA (76.7% and 61.9% vs. 43.2%, respectively; $p < 0.01$). In addition, employed and self-employed parents reported higher intentions for their child would to receive the COVID-19 vaccine (52.9% and 59.7% respectively), whereas parents on a national social assistance programme showed lower intentions (18.2%; $p < 0.01$).

Among caregivers whose children were fully vaccinated according to their national vaccination schedule, 56.3% indicated they were willing to get the COVID-19 vaccine for their child. Caregivers who vaccinated their children against flu in the 2019–2020 and 2020–2021 seasons were also more likely to vaccinate them against SARS-CoV-2 in the future (73.4% and 79.5%, respectively; $p < 0.01$). Interestingly, most (72.5%) caregivers stated that the COVID-19 pandemic did not affect their decision regarding influenza vaccination.

Country-by-Country variations

In respect to the flu vaccine uptake, Greece reported the highest vaccination rates, with uptake rising from 79% in 2019–2020 to full coverage (100%) in 2020–2021 (Table 1). Israel followed, with uptake increasing slightly from 47% to 50%. Italy also reported a significant improvement, rising from 14% to 43%. In Central and Eastern Europe, Slovakia saw a notable increase from 4% to 33%, and Slovenia from 9% to 28%. Croatia remained stable, with uptake moving only slightly from 26% to 28%. By contrast, Russia showed persistently low uptake (9% to 7%). Interestingly, in 2021 the lowest uptake was recorded in Turkey with a percentage of 1.1% ($p < 0.01$).

Differences in intention to administer a COVID-19 vaccine were also observed among participating countries. Caregivers of Polish, Italian and Greek origin stated the strongest willingness (78.6%, 75% and 72.4%, respectively), whereas those from Russia indicated the least (16.7%).

Discussion

Children with IRDs are more vulnerable to infections compared to healthy individuals, due to the underlying disease and immunosuppressive treatment [25, 26]. Routine immunisations according to national vaccination schemes prevent infectious diseases in general and in this target group. Despite the growing knowledge regarding the safety and immunogenicity of routine vaccines in paediatric patients with IRDs, including the influenza vaccine [27], vaccine hesitancy has become a major public health concern, worldwide [28]. Regarding the influenza vaccine, the limited data available concerning vaccine uptake in this priority group, indicate suboptimal coverage [29].

This study demonstrated that only a quarter of JIA patients received the influenza vaccine during the 2020–2021 season. Parental concerns were primarily centred on vaccine safety and side effects. In addition, some caregivers reported they were not aware that their children should receive the vaccine. These findings are consistent with a study that described reasons for influenza vaccine drop-out [30]. Structural barriers such as healthcare access and vaccine supply should also be acknowledged as leading reasons for no vaccination. In our cohort, 12.5% of non-vaccinators reported that the influenza vaccine was unavailable, suggesting that systemic issues continue to hinder uptake even among willing families. Such obstacles may reflect fragmented vaccine supply chains, regional shortages, or challenges in integrating seasonal influenza vaccination into routine paediatric rheumatology care. Importantly, the impact of these supply-related issues may be magnified by limited communication between caregivers and healthcare providers, as over half of non-vaccinators in our study did not have the opportunity to discuss vaccination with a specialist.

Several demographic factors showed to influence vaccine uptake among the participants in our study. Socioeconomic factors such as caregivers' employment and education status were strongly associated with higher vaccine uptake. In detail, employed and self-employed parents were more likely to vaccinate their children against both influenza and COVID-19 compared to unemployed parents. Similarly, parents with tertiary education were also more prone to vaccinate their offsprings compared to those with lower educational levels. Interestingly, families on national social assistance programmes were less likely to pursue vaccination.

Of note, the most important, trusted source of information about influenza vaccine for children shown in our study was the child's paediatric rheumatologist or paediatrician, supported by the literature which showed

that paediatric healthcare providers have a key role in promoting and providing influenza vaccination for children [31]. Thus, healthcare provider influence is probably one of the most significant factors contributing to vaccine uptake. This is also demonstrated in our cohort by the significant increase of influenza vaccine uptake in 4 participating centres which probably provided dedicated vaccination campaigns to their patients' caregivers. Moreover, in support of previous studies, transparent communication and clinician advocacy during routine visits had a strong positive impact on vaccine acceptance [32].

The current study found that a child's history of influenza vaccination and adherence to the national immunisation schedule were significantly correlated with the likelihood of receiving a flu vaccine. This observation is in line with existing research indicating that past behaviour is a solid indicator of future actions in a variety of health activities, including vaccination [33].

In view of the COVID-19 pandemic, experts have warned that the convergence of COVID-19 and seasonal influenza could result in considerable morbidity and mortality [34]. Paediatric vaccination against flu has been considered an important way to attenuate a dual influenza and COVID-19 epidemic [35, 36]. Possibly due to the widespread consequences of the pandemic, the COVID-19 pandemic has fostered some health-protective behaviours, including social distancing, masking, and rigorous hand washing. However, it remains unclear whether it also affected attitudes towards immunisations in general.

A significant increase in flu vaccine uptake was noted in our cohort between the seasons before (2019–2020) and during (2020–2021) the COVID-19 pandemic, despite wide variations among participating countries. Our results suggest that seasonal influenza vaccination rates may be increased because of the ongoing COVID-19 pandemic. In addition, the increased vaccine uptake can also be attributed to the fact that most of the cohort filled the questionnaire in both flu seasons and thus, the vaccine uptake has improved in the second season thanks to raising awareness by the paediatric rheumatologist. These presumptions require careful consideration as other factors might have contributed to higher flu vaccination coverage. Finally, the reasons for the differences noted among countries demand further research.

Regarding a family's intention to have their child immunized against SARS-CoV-2, little is known about parental hesitancy for COVID-19 vaccines for children. In a study published in January 2022, researchers noted a high intention to vaccinate among adult patients with IRDs [37]. Little information is available regarding the intention for COVID-19 vaccine administration of children with IRDs [38, 39]. The present study demonstrated that more than half of the participants reported that it is likely their child will receive the COVID-19 vaccine.

Our study revealed notable differences in influenza and COVID-19 vaccination uptake across JIA subtypes, suggesting that disease characteristics, treatment regimens, and parental perceptions may all play an important role in forming vaccine decisions. For influenza vaccination, children with psoriatic JIA and poly-articular JIA had the highest uptake, while those with undifferentiated JIA had the lowest. One possible explanation is that poly-articular and psoriatic JIA are often associated with more persistent disease activity and systemic treatment, which may increase both physician recommendations and caregiver awareness of infection risk. Regarding COVID-19 vaccination, intention varied significantly between subtypes. Caregivers of children with psoriatic JIA and ERA expressed the strongest willingness to vaccina. Surprisingly, about half of the parents of children with systemic JIA expressed their concerns against COVID-19 vaccine administration, despite the evidence that infections are a known risk-factor for a flare [40]. It is plausible that concerns about vaccine safety in the context of systemic disease, combined with the frequent use of advanced immunosuppressive regimens (e.g., IL-1 and IL-6 inhibitors), may fuel hesitancy among caregivers. In addition to the aforementioned, subtypes requiring closer medical follow-up, such as poly-articular JIA, likely benefit from more frequent provider-led vaccination discussions, while conditions perceived as milder or more fragile may paradoxically result in lower uptake. Addressing these subtle concerns — particularly the fears surrounding systemic JIA — will be crucial for improving vaccine coverage in this vulnerable population.

Finally, the child's previous influenza vaccination status and being fully vaccinated according to their country's vaccination schedule were related to higher likelihood of the child getting a SARS-CoV-2 vaccination. This finding supports the premise that past vaccination behaviour is a strong predictor of future behaviour.

Variations among countries in terms of attitudes toward Influenza and COVID-19 vaccination suggest that while disease-related vulnerability shapes caregiver perceptions everywhere, health policy, vaccine mandates and cultural factors strongly mediate actual vaccination intentions. For instance, the contrast between Greece and Turkey illustrates how system-level and culture can lead to divergent vaccination outcomes, even within geographically proximate countries. In Greece, near-universal influenza uptake was achieved, likely due to strong alignment between national immunisation policy and specialist practice, high availability of vaccines at no cost, and strong caregiver trust in physician advice. By contrast, Turkey reported the lowest influenza vaccination rate, reflecting limited integration of influenza

vaccination into health-care routine, potential financial barriers, and persistent cultural hesitancy toward seasonal influenza vaccination. Notably, in Turkey childhood vaccination is not compulsory, affecting the perception of vaccine uptake in total. Likewise, Russia showed the lowest level of willingness for vaccination against COVID-19. Maybe this is due to widespread skepticism toward COVID-19 vaccines, politicization of pandemic responses, and lower confidence in healthcare authorities [41].

This study has some limitations. Data regarding the vaccine uptake history was self-reported. While caregivers' reports are generally considered reliable, the possibility of underreporting or overreporting cannot be excluded. Another limitation was the variable proportion of JIA subtypes from participating countries since disease type and severity seem to affect vaccination uptake. In addition, unequal sample sizes across the nine participating countries may have influenced the strength of cross-country comparisons. Countries with larger cohorts, such as Greece and Israel, contributed more robust data, whereas findings from countries with smaller samples may not fully reflect national vaccination practices.

To the best of our knowledge, this is the first study to investigate the impact of the COVID-19 pandemic on vaccination intentions against both influenza and COVID-19, and the decision-making factors among children with JIA. Increasing vaccine uptake and compliance for children with IRDs might be achieved by providing appropriate messages and special arrangements for vaccine delivery. Convincing outreach to parents and children is needed to address influenza vaccine hesitancy and to further strengthen the intention to obtain COVID-19 vaccination. As vaccine safety including side effects were the main parental concerns, a clear message about its safety for paediatric patients with IRDs is crucial. It is very important for paediatricians and paediatric rheumatologists to advocate influenza and COVID-19 vaccines for children, during routine visits. Other approaches to address parental hesitancy and further reinforce vaccine acceptance might include using reminder communications, "narrative medicine" techniques, and developing social norms through media campaigns [42].

Conclusions

Despite the high rates of parental hesitancy for influenza immunisation noted in this study, a significant increase in influenza vaccine uptake between the seasons pre-COVID-19 and during the COVID-19 pandemic was reported by this multi-centre cohort of parents of JIA patients from 9 countries. A strong intention for COVID-19 vaccine administration in the context of the COVID-19 pandemic was noted in the families of children with JIA. This study highlights the need to strengthen health education regarding influenza vaccination in high-risk groups, since family physicians and paediatric rheumatologists are noted to be the key trusted source of information about vaccines. Thus, they may play a critical role in promoting vaccination and in achieving universal vaccine coverage both against influenza and SARS-CoV-2 in children with JIA and other IRDs.

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Author contributions
DM, PT and MHB drafted the study and the article. All authors contributed to the data collection and review of the manuscript.

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Data availability
No datasets were generated or analysed during the current study.

Declarations

Ethics approval and consent to participate
The study protocol was approved by the Ethics Committees of all participating centers. All participants were informed about the objectives of this study and its data protection and privacy policies. After providing informed consent, participants completed the questionnaire.

Competing interests
The authors declare no competing interests.

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