

Since January 2020 Elsevier has created a COVID-19 resource centre with free information in English and Mandarin on the novel coronavirus COVID-19. The COVID-19 resource centre is hosted on Elsevier Connect, the company's public news and information website.

Elsevier hereby grants permission to make all its COVID-19-related research that is available on the COVID-19 resource centre - including this research content - immediately available in PubMed Central and other publicly funded repositories, such as the WHO COVID database with rights for unrestricted research re-use and analyses in any form or by any means with acknowledgement of the original source. These permissions are granted for free by Elsevier for as long as the COVID-19 resource centre remains active.

#### Vaccine 40 (2022) 1829-1836

Contents lists available at ScienceDirect

# Vaccine

journal homepage: www.elsevier.com/locate/vaccine

# Exploring the attitudes, concerns, and knowledge regarding COVID-19 vaccine by the parents of children with rheumatic disease: Cross-sectional online survey

Özlem Akgün<sup>a</sup>, Gülşah Kavrul Kayaalp<sup>a</sup>, Fatma Gül Demirkan<sup>a</sup>, Figen Çakmak<sup>a</sup>, Ayşe Tanatar<sup>a</sup>, Vafa Guliyeva<sup>a</sup>, Hafize Emine Sönmez<sup>b</sup>, Nuray Aktay Ayaz<sup>a,\*</sup>

<sup>a</sup> Department of Pediatric Rheumatology, İstanbul Faculty of Medicine, İstanbul University, İstanbul, Turkey <sup>b</sup> Department of Pediatric Rheumatology, Kocaeli School of Medicine, Kocaeli University, Kocaeli, Turkey

#### ARTICLE INFO

Article history: Received 13 August 2021 Received in revised form 27 January 2022 Accepted 31 January 2022 Available online 4 February 2022

Keywords: Vaccine acceptance COVID-19 COVID-19 vaccine Vaccine hesitancy Pediatric rheumatic disease



*Background:* Vaccination programs are effective strategies in preventing infectious diseases and controlling epidemics. Vaccination against SARS-CoV-2 in children has not yet been approved globally, and it is unclear what attitude families will take when it is approved in children. We aimed to investigate the underlying causes of vaccine acceptance, hesitation, and refusal, as well as concerns about the acceptability of the COVID-19 vaccine by parents of children with rheumatic diseases.

*Methods:* Parents of children followed up with a diagnosis of rheumatic disease in the pediatric rheumatology outpatient clinic of a university hospital were included in the study. We applied a closed webbased online survey conducted cross-sectionally and sent to the participants via mobile smartphones.

*Results*: For fathers, mothers, and their children, acceptance rates for a COVID-19 vaccine were 64.2%, 57.7%, and 41.8%, respectively. In the multivariate analysis, factors affecting parents' acceptance of vaccines for their children were as follows: "Receiving antirheumatic medications regularly (AOR 5.40, 95% CI 1.10–26.33, p = 0.03), the previous history of getting special recommended vaccines (AOR 4.12, 95% CI 1.12–27.85, p = 0.03), relying on vaccines for ending pandemic (AOR 8.84, 95% CI 2.80–27.85, p = 0.001), complying with the pandemic measures entirely (AOR 5.24, 95% CI 1.46–18.74, p = 0.01)". The two most common reasons for vaccine rejection were fear of the side effects of the vaccine and its possible interaction with rheumatic drugs used by children.

*Conclusion:* According to our survey, parents were more likely to accept a COVID-19 vaccine for themselves than their children. The success of COVID-19 vaccination programs sources highly on people's willingness to accept the vaccine. It is crucial to vaccinate children for achieving herd immunity and in terms of avoiding vaccine hesitancy. Larger data examining the causes of concerns in parents of both healthy children and children with chronic diseases should be delineated.

© 2022 Elsevier Ltd. All rights reserved.

# 1. Introduction

The COVID-19 was declared a pandemic by the World Health Organization in March 2020 and continues to have a devastating impact on healthcare, educational, social, and economic issues around the world [1]. COVID-19 is currently responsible for over 350 million infections, of which approximately 5,6 million are fatal (1.58%) and therefore remains a serious threat worldwide. According to the most recent national statistics from American Academy

\* Corresponding author at: İstanbul Faculty of Medicine, İstanbul University, Department of Pediatric Rheumatology, Fatih, Istanbul, Turkey.

E-mail address: nurayaktay@gmail.com (N.A. Ayaz).

of Pediatrics, pediatric cases now account for 18.4% of all confirmed COVID-19 cases. According to the same data, the hospitalization rate was reported as 0.1–1.5 and the death rate nearly as 0.25% [1,2]. The expeditious spread of SARS-CoV-2 infection worldwide and the severity of some COVID-19 cases have revealed the global effort towards effective preventive strategies, including vaccine development and mass vaccination programs.

Even though COVID-19 has a relatively milder course in children than adults, reports indicate that severe disease patterns requiring hospitalization and intensive care may come up in children, particularly in patients with comorbidities [3–5]. Multisystem inflammatory syndrome in children (MIS-C), a SARS-CoV-2 infection-related and potentially fatal condition characterized by







fever, hyperinflammation, and shock may lead to morbidity and mortality [6,7]. Furthermore, children might be a significant source of viral transmission and their immunization against SARS-CoV-2 can facilitate the containment of the pandemic [8,9].

Vaccination programs are effective strategies in preventing infectious diseases and controlling epidemics, however, the success of these programs relies on people's understanding and acceptance of the virtue of vaccination. Unwillingness to vaccinate is a serious problem with far-reaching and devastating effects, as seen in previous vaccination programs against other infectious diseases. Various debates about safety and efficacy in scientific and nonscientific literature can impair trust in vaccines [10].

Until now, plenty of studies regarding adult's perception, knowledge, and intention against COVID-19 vaccines were performed and a systematic review about confidence and receptivity for COVID-19 vaccines in adults was published at the end of 2020, analyzing some selected studies reporting COVID-19 vaccine receptiveness in detail by paying heed to factors influencing the attitudes of the participants. Few studies about the willingness of parents and caregivers to vaccinate their children against COVID-19 were issued however; these cohorts were not chosen from children with any of the well-known chronic diseases [11,12].

The immune dysregulation of children with rheumatic diseases (pedRD) due to both their underlying conditions and antirheumatic drugs they used may render them susceptible to infections.

Initially, on December 11, 2020, FDA authorized an Emergency Use Authorization (EUA) for the BNT162b2 mRNA vaccine for adolescents aged  $\geq$  16 years and subsequently, on May 10, 2021, the age range was expanded to 12–15 years [13]. The highly contagious variants of SARS-CoV-2 and the possibility of these variants escaping neutralizing antibodies have raised new concerns about vaccination. In a study evaluating the impact of different vaccine administrations on variants, the heterologous prime–boost approaches (combination of two doses of CoronaVac and BNT162b2 mRNA vaccine booster dose) was shown to induce high virus-specific antibody levels and potent neutralizing activity against the ancestral virus and Delta variant [14]. The studies from the UK, Canada and Qatar demonstrated that BNT162b2 mRNA vaccines are over 90% effective in preventing severe infection against the Delta variant [15–17].

Iwasaki et al. have reported inadequate antibody response to the Omicron variant in the participants receiving a two-dose CoronaVac vaccine regimen. Regardless of whether the initial vaccination is homogeneous or heterogeneous, inactivated or mRNAbased, data support the administration of a booster dose for enhancing the antibody response to Omicron variant [17,18].

We aimed to investigate the concerns regarding COVID-19 vaccine and its acceptability by the parents of pedRD, as well as the decisive background features of vaccine acceptance, hesitancy and refuse status, and to delineate parents' knowledge and sources of information regarding COVID-19 vaccines.

#### 2. Materials and methods

#### 2.1. Participants and data collection

A closed web-based online survey conducted cross-sectionally by the Google Forms software (Google Forms, Albuquerque, New Mexico, USA) was sent to the participants via a WhatsApp link by mobile smartphones. The survey was tested on 25 parents before sending it to the whole cohort. After discarding these pilot replies and duplicated entries, the remaining replies were checked for the completeness of the responses to the questions. Incomplete questionnaires were neglected. The survey was sent to parents of 540 patients with pedRD who attended the Istanbul University Istanbul Medical Faculty pediatric rheumatology outpatient clinic within the last 6 months. Patients whose diagnosis was uncertain or at the stage of diagnosis were not included in the cohort.

Either the mother or the father of 201 children answered the online survey. If more than one child followed with pedRD is present in the family, parents only answered the questionnaire once.

Patients included in the study were divided into 4 groups according to their diagnosis; familial Mediterranean fever (FMF), juvenile idiopathic arthritis (JIA), resistant FMF, and other periodic fever syndromes (PFS), vasculitis, and connective tissue diseases (CTD).

The survey included 38 questions and consisted of six sections; the informed consent form, questions about socio-demographic data, the general health status of the child, COVID-19 related information, pandemic protection measures, and the knowledge concerning vaccines developed against SARS-CoV2 infection.

Data regarding specific diagnoses used for their pedRD were attained from the electronic files of the patients.

In the informed consent form section; participants were informed that taking part in the survey is voluntary; they have the right to refuse to be involved in the study. Their personal contact information and names will be kept confidential and the information will only be used for scientific research purposes. By marking the consent form button as "yes", they indicated that they wanted to be included in the study.

In the socio-demographic data section; the age of the patient, the age of the mother and father, the educational status and employment status of the parents, the number of people in the family living in the same house, the presence of an individual  $\geq$  65 years of age in the same house with the family were questioned. Our patients were in the 3–18 years of age with a median age of 12 years. According to the visual binning analysis performed in the SPSS, the patients were divided into 3 groups:  $\leq$ 5 years, 6–11 years and 12–18 years. The educational statuses of parents were classified as primary school, high school, and university/ higher graduate. Mothers, fathers, and children were classified according to age groups. Mothers and fathers were divided into three age groups: 20–35 years old, 36–45 years old and over 45 years old.

In the general health status of the child information section; the regular reception of medications during the pandemic process, the vaccination status by the national mandatory vaccination program, a flu shot experience in the previous season were questioned. In case of the application of recommended special vaccines (*rotavirus* vaccine, meningococcal serogroup B vaccine, meningococcal serogroup A, C, W, Y vaccine, human papillomavirus vaccine), the replies were marked as "I had all of them", "I had some of them", and "I hade none of them".

In the Covid-19 related information section; parents were asked to mark what kind of disease Covid-19 is from the choices as "Covid-19 is a deadly illness", "a more severe illness than flu", "a flu-like illness", asked for the history of COVID-19 and presence of deaths due to COVID-19 in the family and/or near environment (the household, relatives, neighbors, and friends).

In the pandemic protection measures section; parents were asked for compliance with pandemic protection measures; questioned about wearing masks in the common area, compliance with hygiene rules, avoiding social and meal gathering in the common area with individuals outside the family. The questions were answered as "yes" or "no".

The knowledge concerning vaccine developed against SARS-CoV2 infection section; parents were asked if they were vaccinated against COVID-19 and if the child will going to be vaccinated after vaccination program took place in Turkey for children. They Ö. Akgün, Gülşah Kavrul Kayaalp, Fatma Gül Demirkan et al.

replied, "yes", "no", "undecided". Those who refused the vaccination and were hesitant were asked why they did not want to be vaccinated. The options were as; "side effects may occur", "I do not trust the vaccine, it may interact with the child's medicines", "it may exacerbate the child's disease", "I do not trust the vaccines coming from abroad", "COVID-19 is already mild in children", "I do not have enough information about the vaccines". Those who accepted the vaccine and were undecided were asked why they accepted it. The options were as; "if I am vaccinated, I may not become ill", "if I get vaccinated, I may have a mild illness", "if I am vaccinated, I may protect my relatives from the disease". They answered "yes" or "no" to the question of whether the pandemic can be controlled with a vaccine. Parents were asked as; "are there people around you who refuse to be vaccinated", "do you follow the news about COVID-19 and its vaccination", "from which source and how often", "are there people who have been vaccinated in your family", "have any side effects developed after vaccination?"

Ethical statement

The survey was made between 06 March and 23 May 2021. It was approved by the Ministry of Health (2021-02-19T01\_45\_05). The study was also approved by the Ethics Committee of Istanbul University Istanbul Medical Faculty (23.06.2021-254233).

#### 2.2. Statistical analysis

Results SPSS software version 21 was used to evaluate the statistical analysis. Continuous data were defined as mean, standard deviation (SD) medians, minimum (min) and maximum (max) values, and categorical variables as percentages. Variables were investigated using visuals (histogram, probability plots) or did not show a normal distribution. Categorical variables were compared with the chi-square test or Fisher's exact test when appropriate. Univariate binary logistic regression analysis was performed on data with a significant p-value in the chi-square test. As a final step, multivariate logistic regression analysis was performed. A pvalue<0.05 was considered to indicate a statistically significant result.

# 3. Results

#### 3.1. Sociodemographic data

Out of 540 participants, 201 (37.2%) have completed the online survey. Of the cohort of children with rheumatic disease, 111 (55.2%) were girls and 90 (44.8%) were boys. The median (min-max) age of the patients was 12 (3–18) years.

The median ages of the mothers and fathers were 38 (22–64) years and 42 (26–64) years, respectively. The education and employment status of the parents and the average monthly income of the family were depicted in Table 1. The household size was categorized as  $\leq$  4 people (51.7 %) and > 4 people (48.3%) living in the same house. An individual over 65 years of age in the family was noted in 11.9 % of the cohort. Parents were grouped according to their age as; 20–35 years, 36–45 years, >45 years (Table 1).

#### 3.2. General health information

Patients were categorized as familial Mediterranean fever (38.3%), juvenile idiopathic arthritis (35.8%), resistant FMF and other PFS under biologic therapy (10.0%), vasculitis, and CTD (15.9%).

During the pandemic, 90.5% of the patients received their medication regularly. The proportion of patients vaccinated in accordance with the national mandatory vaccination program was 92%. Among the cohort, 59.2% of children did not get any recommended special vaccines; however, 40.8% had some or all of these special vaccines. As a recommended special vaccine, 9 (4.5%) patients had influenza vaccine during the last season (Table 2).

#### 3.3. Data on COVID-19 disease

When it was questioned how parents comprehend Covid-19; 75.1% stated that "*it was a fatal disease*", 21.9% said "*it was a more severe disease than the flu*", 3% thought "*it was a flu-like illness*". The proportion of families with SARS-CoV-2 was 24.8%. The rate of deaths due to COVID-19 in the family and/or close circle (the household, relatives, neighbors, and friends) was 44.3 %.

#### 3.4. Measures related to the pandemic

The rate of compliance with the rule of wearing a mask in the common areas was 98.5%, avoiding crowded environments was 94.5%, paying attention to hand hygiene was 97.0%, avoiding social and meal gatherings with other people than those living in the same house was 43.8%. Parents of 81 (40.3%) children claimed that they totally complied with all the measures related to the pandemic.

3.5. The knowledge concerning vaccine developed against SARS-CoV2 infection section

In Table 2, the answers regarding questions of COVID-19 vaccine is outlined. Fathers' vaccination acceptance rate for themselves was 64.2%, and mother's vaccination acceptance rate for themselves was 57.7%. The reasons for accepting and rejecting the vaccine for the children of participants are seen in Fig. 1A and Fig. 1B and the rate of participants who refused, hesitated, or accepted the vaccine were depicted in Fig. 2.

The sources of news received about vaccines were asked and shown in Fig. 1C; Participants followed news about vaccines 66.2% "every day", 24.4% "few days a week", 3.0% "once in a month" and, 6.5% "don't follow specifically".

The group with the highest vaccine acceptance rate was parents of the children with the diagnosis of vasculitis and connective tissue diseases (56.3%, 18/32).

# 3.6. Vaccine acceptance status

Of the parents in the cohort, 41.8 % accept, 45.8 % were hesitant, and 12.4 % reject to vaccinate their child against COVID-19.

Vaccine acceptance rates for parents themselves and their children are indicated in Table 3 and Fig. 2.

Age and education level of the parents, total monthly income of the families, number of people living in the same house, presence of COVID history, and also deaths due to COVID-19 in the family and/or close circle (the household, relatives, neighbors, and friends), and, presence of individuals over 65 years in the same house with the family were not significant risk factors in terms of vaccine acceptance (Table 1).

Vaccination status according to the national mandatory vaccination program was not found as a significant factor in predicting vaccine acceptance [the ones who have completed (77/185; 41.6%) and the ones who have not completed their mandatory vaccination schedule (7/16; 43.8%) (p = 0.98)]. Vaccination with the flu vaccine in the past season did not make any change in the acceptance of COVID-19 vaccines (4/9; 44.4% had influenza, % p = 0.10). Six parents (3%) consider COVID-19 as a simple illness like flu, 195 parents figure out COVID-19 either as a fatal disease (75,1%) or a disease worse than flu (21.9%), however these perceptions were not endorsing vaccine acceptance status (Fisher exact test p = 1.0).

# Table 1

Demographics, socioeconomic and household vaccination status of participants.

Characteristics		N = number	n=%	Vaccine accept (p value)
Gender				0.42
	Female	111	55.2	
	Male	90	44.8	
Age groups of patients				0.07
	$\leq$ 5 years old	13	6.5	
	6–11 years old	83	41.3	
	12–18 years old	105	52.2	
Age groups of mothers				0.19
	20–35 years old	73	36.3	
	36–45 years old	99	49.3	
	>45 years old	29	14.4	
Age groups of fathers	-			0.22
	20-35 years old	32	15.9	
	36-45 years old	114	56.7	
	>45 years old	55	27.4	
Father's educational status	5			0.37
	Primary education	119	59.2	
	High school (lycee)	49	24.4	
	University, graduate	33	16.4	
Mother's educational status	3,0			0.56
	Primary education	136	67.7	
	High school (lycee)	39	19.4	
	University, graduate	26	12.9	
Family's common monthly income				0.54
	<5000 TL (€478)	144	71.6	
	>5000 TL (€478)	57	28.4	
Is there an individual over 65 years of age in the family?	· 5000 IE (01/0)	51	20.1	0 38
is there an marriadal over os years of age in the family.	Ves	24	119	0.50
	No	177	88.1	
How many people live in your house?	110	1//	55.1	0.97
now many people live in your nouse:	4 or less	104	517	0.57
	5 or more	07	/83	
	5 OF HIDE	57	40,5	

#### Table 2

Questions regarding compliance with COVID-19 disease, general health information of children and pandemic measures.

Have you been vaccinated in accordance with the Ministry of Health vaccination schedule?				0.98
	Yes	185	92	
	No	15	8	
Has your child been applied influenza vaccine in the last season?				0.10
	Yes	9	4,5	
	No	192	95,5	
What do you think about COVID-19 disease?				1.0 (Fisher exact test)
	Fatal	151	/5.1	
	Worse than the flu	44	21,9	
Use servers had CARC CaV 2 infection in the household?	Like the flu	6	3	0.07
Has anyone had SARS-Cov-2 infection in the household?	Vac	121	65.2	0.27
	Yes	131	24.0	
Did anvone die in vour closed circle from COVID 102	NO	70	54.0	0.26
Did anyone die in your closed circle noin covid-15?	Did not happen	89	443	0.20
	Household relatives	62	30.8	
	Friend neighbor	50	24.9	
Are you wearing a mask in common areas?	incha, neighbor	20	2 110	0.26
	Yes	198	98.5	
	No	3	1.5	
Are you avoiding crowded environments?				0.10
	Yes	190	94,5	
	No	11	5,5	
Are there any people in your closed circle who refuse or hesitant about vaccines?				0.79
	Yes	113	56.2	
	No	88	43.8	
Is there anyone who have been vaccinated in the household?				0.61
	Yes	70	34.8	
	No	131	65.2	
Are you following the news on pandemic and COVID-19?				0,87
	Yes	185	92	
Here the state of the second state of the second sector	NO	16	8	0.47
How often do you follow the news about the pandemic?	Friender	125	67.2	0.47
	Everyddy One or two dawr a week	135	07.2	
	Once in a week	40 5	25.9 25	
	I don't particularly follow	12	2.5	
	i don't particularly 10110W.	15	0.5	

#### Ö. Akgün, Gülşah Kavrul Kayaalp, Fatma Gül Demirkan et al.



Fig. 1. Causes of vaccine accept and refuse, obtaining route of COVID-19 information.



Fig. 2. Acceptance, refuse, and hesitancy of parents for themselves and their children.

#### Table 3

COVID-19 vaccination status of closed circle of parents.

	Answer "yes" (%)	n/N	P value
Are there people around you who refuse or hesitant to be vaccinated for COVID-19?	56.2%	45/201	0.79
Is there any one who has been vaccinated for COVID-19 in your family?	34.8%	70/201	0.24
Are there people with any side effects developed after COVID-19 vaccination in your family?	12.8%	9/70	0.64 (Fisher's exact)

COVID-19, Coronavirus disease 2019

The presence of an individual in the family who has been vaccinated against COVID-19, the presence of vaccine refusal or hesitancy in the near environment of the parents, and close followup of the vaccination news was not found to be related to vaccination acceptance status (p = 0.61, p = 0.79, p = 0.79, respectively). On the other hand, parents who believed that the pandemic will end with a vaccine had significantly higher rates of vaccine acceptance than those who did not believe (p < 0.001).

The highest rate of vaccine acceptance was recorded in the families of children with vasculitis and CTD (56.3%), followed by FMF 41.6%, 36.1% JIA, 40% resistant FMF and other PFS under biologic therapy. Factors affecting children's vaccination acceptance status in univariate binary logistic regression analysis; use of antirheumatic medications regularly (AOR 4.98, 95% CI 1.37–18.09), previous history of getting special recommended vaccines (AOR 3.63, 95% CI 1.24–10.59), avoiding social and meal gatherings with other people in common areas with people outside the family (AOR 2.57, 95% CI 1.001–6.61), paying attention to hand hygiene during the pandemic (AOR 15.82, 95% CI 1.67–148.95), relying on vaccines for ending pandemic (AOR 8.17, 95% CI 3.04–21.99), complying with all the pandemic measures (AOR 3.17, 95% CI 1.15–8.71), was significantly associated with acceptance of vaccination of their children against COVID-19 (Table 4).

A forward step logistic regression analysis was performed with a dichotomized version of vaccination against COVID-19 for pedRD as a discrete variable and quantitative findings/factors (use of antirheumatic medications regularly, the previous history of getting specially recommended vaccines, relying on vaccines for ending pandemic, complying with all the pandemic measures, avoiding social and meal gatherings with other people in common areas with people outside the family, paying attention to hand hygiene during the pandemic) associated with COVID-19 vaccine acceptance for the child. The final model included the first four predictive variables and predicted significantly 'acceptance probability' (omnibus chi-square = 34.64, df = 4, p < 0.001). The questions related to avoiding social and meal gatherings with other people in common areas with people outside the family, paying attention to hand hygiene during the pandemic did not significantly predict the 'acceptance probability', so they were excluded from the

Table 4	
---------	--

Affecting factors of COVID-19 vaccine embracement.

	Univariate regression model			Multivariate regression model		
	OR	95% CI	р	OR	95% CI	р
May a pandemic be prevented with a vaccine?	8.17	3.04-21.99	<0.001	8.84	2.80-27.85	<0.001
Did your child receive their antirheumatic drugs regularly during the pandemic process?	4.98	1.37-18.09	0.014	5.40	1.10-26.33	0.037
Did your child have the recommended vaccines that are not included in the national vaccination calendar?	3.63	1.24–10.59	0.018	4.12	1.12-15.08	0.032
Did you fully comply with the pandemic measures?	3.16	1.15-8.71	0.026	5.24	1.46-18.74	0.011
Did you pay attention to hand hygiene?	15.8	1.67-148.95	0.016			
Did you avoid social and meal gatherings with other people than those living in the same house?	2.57	1.00-6.61	0.05			

OR, odds ratio; CI, confidence interval; P value, statistical significance.

model. The Hosmer-Lemeshow test shows that the model adequately fits the chi-square = 3.65, DF = 6, p = 0.72 data (Table 4).

#### 4. Discussion

In pursuance of herd immunity to be effective, vaccines should be administered to all age groups expeditiously. However, vaccine acceptance and actual vaccination behavior of parents for their children may be divergent as experienced in the H1N1 pandemic [19]. Therefore, grasping parents' perspectives regarding vaccines is crucial for both policymaking and service planning.

Vaccination of children is of greater importance in countries where the population under the age of 18 is dense. Children are generally getting over COVID-19 with fewer and milder symptoms; however they are the potent spreaders of the disease as they pay less attention to the mask, distance and hygiene rules than adults. Crowded social areas such as schools enhance the risk even more. Since education is an indispensable element for children, vaccination seems to be the most effective weapon of protection against school absenteeism with the expansion of real-life data regarding the efficacy and safety of vaccines in children, concerns about vaccination may diminish.

In this study, the acceptability, hesitations, rejections, and factors influencing the attitudes of the parents towards COVID-19 vaccination, likewise, the knowledge and sources of information regarding COVID-19 vaccination were assessed with a web-based survey. To our knowledge, among children with RD this is the first research of its kind raising information from families on a patientby-patient basis in particular.

When the families were asked about their self vaccination status, fathers had a higher rate of acceptance than the mothers (64.2% vs 57.7%) [11,20], however, the difference was not significant statistically. In the previous studies, acceptance rate of COVID-19 vaccination is higher for males than the females as well; however, there are some contradictory results in the literature [12,21,22]. The fact that the disease causes increased mortality and morbidity in men may explain their higher rate of vaccine acceptance [23].

In European countries like Denmark and England, vaccine acceptance rates in adults were around 80% and in France, one of the most vaccine-hesitant countries in the World, the rate was about 60% [21,24]. In this survey, while the parents were vaccinated against COVID-19 with a higher rate, the acceptance rate of vaccination was lower for their children and more than half of them were either hesitant or rejecting the vaccination after its approval for children. Our results were similar to a previous survey conducted in the United Kingdom (UK) among parents and guardians on the acceptability of a future vaccine for themselves and their children, this study, reveals vaccination acceptance rates of 55.8% for parents themselves and 48.2% for their children [25]. Participants of the survey reported that it was less risky to vaccinate adults than children as the vaccine trials were carried on adults.

Likely, the major argument of the parents against vaccination in our cohort was the expectation of side effects. As with many vaccines, COVID-19 vaccines have various side effects such as thrombocytopenia, rash, anaphylaxis, and Guillian Barre syndrome. One of the most discussed side effects was myocarditis, especially after the second dose of BNT162b2 vaccine. Although several studies have reported an increased risk of myocarditis, the vaccination program has not been interrupted. According to the Vaccine Adverse Event Reporting System (VAERS), between December 14 and 2020-July 16, 2021, approximately 8.9 million U.S. adolescents aged 12-17 years had received BNT162b2 vaccine and 9,246 adverse events were reported of which 90.7% were non-serious and 9.3% were serious, including myocarditis [13,26]. In a recent study, 2260 adolescents under 16 years were grouped in the arm of BNT162b2 vaccine or placebo receivers, no serious side effects were observed except for pain at the injection site, fatigue, and headache [27]. The benefit-risk balance between the prevention of severe symptomatic illness, hospitalization, mortality and morbidity due to COVID-19 and the cardiac risks of COVID-19 vaccines seems to be in favor of vaccination.

However, our study was conducted among children with RD under various immunsuppresives, and the second factor for not accepting the vaccination was the probability of interactions between vaccines and the medications. A small number of parents carried the thought that vaccines may cause exacerbations of their children's rheumatic condition. Interestingly, 55% of parents claimed that they refuse because they lack information about COVID-19 vaccines. This issue should be addressed in the priority of the authorities and policymakers, since organized and wellconstructed approaches in collaboration with health care professionals may hinder hesitancy against vaccination. Overall, as the time passed since the outbreak of pandemic, and news about severe course of COVID-19, like MIS-C presentations in children spread, only 13.1% of parents in our cohort recognized COVID-19 being a milder disease in children as a factor for refusing the vaccines. It seems that, although they are short of knowledge regarding vaccines, they are more aware of the course of COVID-19 in children.

In a study performed in China, parental acceptability of COVID-19 vaccination for children under the age of 18 years was investigated, and the prevalence was 72.6%. The higher COVID-19 vaccine acceptance rate was attributed to the theory of planned behavior (TBP) applied as a theoretical framework. Facing with the positive information related to COVID-19 in the previous months was reported by 69.3% of the participants [28]. The authors claimed that besides personal and social influences, the information given via media and social media may drive parents in the expected directions. Likewise, in our survey, the major sources of pandemic news where parents get were ordered as television, internet, and social media. Accordingly, for enhancing positive attitudes towards vaccination, benefitting from these sources may be employed as operational health promotion techniques. In a Turkish study conducted in adults with rheumatic diseases, the information sources of the general population and health care workers regarding both COVID-19 and COVID-19 vaccine were questioned, answers were lined up as television (72.8%), social media (58.1%), and friends (10.1%) [29]. Despite the fact that the media is a strong instrument for distributing information, there are worries about erroneous data, unsubstantiated hearsay, and even malicious misinformation on these platforms [23–25], which could offer issues for future COVID-19 immunization efforts. So, strict supervision of these sources of information by the relevant institutions and sharing the data obtained from scientific studies with the public in a transparent manner seem to be essential.

A cross-sectional survey reported the willingness of caregivers to vaccinate their children against COVID-19 as 65.2%. Of these children, 12% had a chronic illness, and although not reaching statistical significance, parents have a lower rate of intent to vaccinate their children [30]. This may be a reflection of the concerns about vaccinating immunsupressed children. In our study, 41.8% of the parents stated that they will accept vaccination of their child and they were timid to vaccinate their children with a rheumatic disease rather than themselves.

Patients with rheumatic diseases are at risk of serious infections due to both immune dysfunctions resulting from their diseases and the usage of immunomodulatory drugs. The presence of a rheumatic disease or the usage of anti-rheumatic drugs may influence the course of SARS-CoV-2 infection. A *meta*-analysis by Akiyama et al. [31] reported that having a rheumatic disease increased the risk of the symptomatic course of COVID-19, rate of hospital admission, and death due to COVID-19 in adult patients when compared to that in the general population. Therefore, it is quite important to protect patients with rheumatologic diseases from infection by vaccination.

In the cohort, parents giving credence to the vaccination for impeding COVID-19 pandemic have a higher rate of acceptance of COVID-19 vaccine for their children. Continuation of regular medications conveniently during the pandemic, having specially recommended vaccines other than mandatory national vaccination program applied beforehand, and retaining in full compliance with the pandemic measures were found significantly correlated with the acceptance of COVID-19 vaccines. It is not surprising that families who regularly use their medications and receive special vaccines that are not in the national vaccination program previously are likely to communicate better with healthcare professionals and be more concerned with the scientific advancements. As expected, acceptance of COVID-19 vaccines is high among those who think that the pandemic will end with vaccination. Although vaccine acceptance was significantly higher in those who paid attention to hand hygiene and avoid social and meal gatherings with people other than the family, these predictor variables were ruled out in the multivariate analysis. The age of children, avoiding crowded places, and social/meal gatherings with other people who did not live together were found as factors affecting vaccine acceptance in the univariate analysis in the study conducted in participants with healthy children [28].

Having a flu shot within the past year has been identified as an important factor for acceptance of the COVID-19 vaccine [30,32]. However, in our cohort, only 4.5% of children had a previous flu shot and while dealing with the recurrent inflammatory attacks of children with rheumatic conditions, physicians may not give ample consideration to the vaccines like influenza that are not in the national mandatory vaccination program, so it wouldn't be appropriate to determine the effect of influenza vaccine on acceptance of COVID-19 vaccination in this cohort.

The reasons to accept vaccination for their children were asked to the families and 3 items that they can choose from more than one were offered. Majority of the participants accepted vaccination because they believed that they won't get COVID-19 or even if they were caught to COVID-19, their illness would be mild. A small portion of the respondents favored vaccination for protecting their relatives from the disease. Similarly, Goldman et al. reported that caregivers accept to vaccinate their children for ensuring their children are immune to SARS-CoV-2 infection [30]. Herd immunity, economic and social benefits came subsequent to protect their children's health. In another study from England, the main reasons of the families for accepting their children to get vaccines were aligned as protecting their children, protecting others, and feeling that vaccination is a means of regaining control of one's normal life [25].

In the literature, it has been shown that the acceptability of the vaccine increases as the education level [33] and the monthly income [34] of the parents increase [35]. In our cohort, the acceptance of vaccination for their children was increased in parents with higher education levels and higher average monthly income, but the difference did not reach significance. Similarly, without being statistically significant, Zhang et al reported high personal income and high education level as factors increasing acceptability rate of COVID-19 vaccination [28].

Our study has some limitations. The fact that it was singlecentered and conducted only with children with chronic rheumatic diseases may limit the generalization of the results to the whole population and other chronic diseases. However, there are limited number of studies consisting of caregivers and parents attitudes towards COVID-19 vaccine and as far as we know this is the first study questioning the acceptability of COVID-19 vaccination for children with rheumatic diseases, so our results may enhance an objective understanding of the attitudes, curtail misinformation of the health care authorities, raise efforts to support vaccine acceptance when they become available for children under 18 years of age.

Secondly, the survey was executed before the approval of vaccines for children, so the results may not meet the final decisions of the families; a follow-up study regarding vaccination rates after approval of the vaccines may reveal presumed divergences between the attitudes and actions towards COVID-19 vaccines dynamically.

# 5. Conclusions

The success of COVID-19 vaccination programs sources highly on people's willingness to accept the vaccine. Parents should be informed more and more accurately about the vaccine, especially the concerns regarding side effects of the vaccines, likely interactions of the vaccines with the rheumatic medications, and exacerbations of their diseases should be elicited and if possible eliminated. In order to lessen concerns, the development steps, efficacy and side effects of the vaccine should be shared with the public in a transparent manner. In consideration of misinformation, well-known and most applied information sources of the families should be arranged by the authorities and policymakers. It is crucial to vaccinate children for succeeding to achieve herd immunity and in terms of avoiding vaccine hesitancy; data of larger, multicentric studies examining the causes of concerns in parents of both healthy children and children with chronic diseases should be delineated.

#### Funding

None.

#### **Declaration of Competing Interest**

The authors declare that they have no known competing financial interests or personal relationships that could have appeared to influence the work reported in this paper.

#### Acknowledgment

None.

# Appendix A. Supplementary material

Supplementary data to this article can be found online at https://doi.org/10.1016/j.vaccine.2022.01.061.

#### References

- WHO: World Health Organization Coronavirus (COVID-19) Dashboard. https://covid19.who.int/ (2021). Accessed.
- [2] Pediatrics AAo: Children and COVID-19: State-Level Data Report. https://www. aap.org/en/pages/2019-novel-coronavirus-covid-19-infections/children-andcovid-19-state-level-data-report/ Accessed.
- [3] Shekerdemian LS, Mahmood NR, Wolfe KK, Riggs BJ, Ross CE, McKiernan CA, et al. Characteristics and Outcomes of Children With Coronavirus Disease 2019 (COVID-19) Infection Admitted to US and Canadian Pediatric Intensive Care Units. JAMA Pediatrics 2020;174(9):868. <u>https://doi.org/ 10.1001/jamapediatrics.2020.1948</u>.
- [4] Castagnoli R, Votto M, Licari A, Brambilla I, Bruno R, Perlini S, et al. Severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) infection in children and adolescents: a systematic review. JAMA Pediatrics 2020;174(9):882–9.
- [5] Ouldali N, Yang DD, Madhi F, Levy M, Gaschignard J, Craiu I, et al. Factors associated with severe SARS-CoV-2 infection. Pediatrics 2021;147(3).
- [6] Feldstein LR, Rose EB, Horwitz SM, Collins JP, Newhams MM, Son MBF, et al. Multisystem inflammatory syndrome in US children and adolescents. New Engl J Med 2020;383(4):334–46.
- [7] Bautista-Rodriguez C, Sanchez-de-Toledo J, Clark BC, Herberg J, Bajolle F, Randanne PC, et al. Multisystem inflammatory syndrome in children: an international survey. Pediatrics 2021;147(2).
- [8] Chan JF-W, Yuan S, Kok K-H, To KK-W, Chu H, Yang J, et al. A familial cluster of pneumonia associated with the 2019 novel coronavirus indicating person-toperson transmission: a study of a family cluster. The Lancet 2020;395 (10223):514–23.
- [9] Laws RL, Chancey RJ, Rabold EM, Chu VT, Lewis NM, Fajans M, et al. Symptoms and transmission of SARS-CoV-2 among children—Utah and Wisconsin, March–May 2020. Pediatrics 2021;147(1).
- [10] Pandolfi F, Franza L, Todi L, Carusi V, Centrone M, Buonomo A, et al. The importance of complying with vaccination protocols in developed countries: "anti-vax" hysteria and the spread of severe preventable diseases. Current Med Chem 2018;25(42):6070–81.
- [11] Fisher KA, Bloomstone SJ, Walder J, Crawford S, Fouayzi H, Mazor KM. Attitudes toward a potential SARS-CoV-2 vaccine: a survey of US adults. Ann Internal Med 2020;173(12):964–73.
- [12] Ward JK, Alleaume C, Peretti-Watel P, Peretti-Watel P, Seror V, Cortaredona S, et al. The French public's attitudes to a future COVID-19 vaccine: The politicization of a public health issue. Soc Sci Med 2020;265:113414. https://doi.org/10.1016/j.socscimed.2020.113414.
- [13] Hause AM, Baggs J, Marquez P, Myers TR, Gee J, Su JR, et al. COVID-19 Vaccine Safety in Children Aged 5–11 Years – United States, November 3–December 19, 2021. MMWR Morb. Mortal. Wkly. Rep. 2021;70(5152):1755–60.

- [14] Pérez-Then E, Lucas C, Monteiro VS, Miric M, Brache V, Cochon L, et al. Neutralizing antibodies against the SARS-CoV-2 Delta and Omicron variants following heterologous CoronaVac plus BNT162b2 booster vaccination. 2022:1-.
- [15] Nasreen S, He S, Chung H, Brown KA, Gubbay JB, Buchan SA, et al. Effectiveness of COVID-19 vaccines against variants of concern. Canada. 2021.
- [16] Bernal J, Andrews N, Gower C, Gallagher E, Simmons R, Thelwall S, et al. Effectiveness of COVID-19 vaccines against the B. 1.617. 2 variant. medRxiv. 2021;24.
- [17] Abu-Raddad L, Chemaitelly H. Butt AJEotBbC-vatB. National Study Group for COVID-19. Vaccination 2021;1(7).
- [18] Ai J, Zhang H, Zhang Y, Lin K, Zhang Y, Wu J, et al. Omicron variant showed lower neutralizing sensitivity than other SARS-CoV-2 variants to immune sera elicited by vaccines after boost. Emerg Microbes Infect 2022;11(1):337–43.
- [19] Ofri D. The Emotional Epidemiology of H1N1 Influenza Vaccination. Emotional Epidemiol H1N1 Influenza Vaccinat 2009;361(27):2594–5.
- [20] Thigpen C, Funk CJUPRC. Most Americans expect a COVID-19 vaccine within a year; 72% say they would get vaccinated. 2020.
- [21] Lazarus JV, Ratzan SC, Palayew A, Gostin LO, Larson HJ, Rabin K, et al. A global survey of potential acceptance of a COVID-19 vaccine. Nature Med 2021;27 (2):225–8.
- [22] Wong LP, Alias H, Wong P-F, Lee HY, AbuBakar S. The use of the health belief model to assess predictors of intent to receive the COVID-19 vaccine and willingness to pay. Human Vaccines Immunotherapeut 2020;16(9):2204–14.
- [23] Remuzzi A, Remuzzi GJTI. COVID-19 and Italy: what next? The Lancet 2020;395(10231):1225-8.
- [24] Neumann-Böhme S, Varghese NE, Sabat I, Barros PP, Brouwer W, van Exel J, et al. Once we have it, will we use it? A European survey on willingness to be vaccinated against COVID-19. Eur J Health Econ 2020;21(7):977–82.
- [25] Bell S, Clarke R, Mounier-Jack S, Paterson P. Parents' and guardians' views on the acceptability of a future COVID-19 vaccine for themselves and their children: cross-sectional survey and qualitative interview data. 2020.
- [26] Hause AM, Gee J, Baggs J, Abara WE, Marquez P, Thompson D, et al. COVID-19 Vaccine Safety in Adolescents Aged 12–17 Years — United States, December 14, 2020–July 16, 2021. MMWR Morb Mortal Wkly Rep 2021;70(31):1053–8.
- [27] Frenck RW, Klein NP, Kitchin N, Gurtman A, Absalon J, Lockhart S, et al. Safety, Immunogenicity, and Efficacy of the BNT162b2 Covid-19 Vaccine in Adolescents. N Engl J Med 2021;385(3):239–50.
- [28] Zhang KC, Fang Y, Cao H, Chen H, Hu T, Chen YQ, et al. Parental acceptability of COVID-19 vaccination for children under the age of 18 years: cross-sectional online survey. JMIR Pediatrics Parenting 2020;3(2).
- [29] Yurttas B, Poyraz BC, Sut N, Ozdede A, Oztas M, Uğurlu S, et al. Willingness to get the COVID-19 vaccine among patients with rheumatic diseases, healthcare workers and general population in Turkey: a web-based survey. JMIR Pediatrics Parenting 2021;41(6):1105–14.
- [30] Goldman RD, Yan TD, Seiler M, Cotanda CP, Brown JC, Klein EJ, et al. Caregiver willingness to vaccinate their children against COVID-19: Cross sectional survey. Vaccine 2020;38(48):7668–73.
- [31] Akiyama S, Hamdeh S, Micic D, Sakuraba A. Prevalence and clinical outcomes of COVID-19 in patients with autoimmune diseases: a systematic review and meta-analysis. Ann Rheumatic Dis 2021;80(3):384–91.
- [32] Guaraldi F, Montalti M, Di Valerio Z, Mannucci E, Nreu B, Monami M, et al. Rate and Predictors of Hesitancy toward SARS-CoV-2 Vaccine among Type 2 Diabetic Patients: Results from an Italian Survey. Vaccines 2021;9(5):460.
  [33] Wong MC, Wong EL, Huang J, Cheung AW, Law K, Chong MK, et al. Acceptance
- [33] Wong MC, Wong EL, Huang J, Cheung AW, Law K, Chong MK, et al. Acceptance of the COVID-19 vaccine based on the health belief model: A population-based survey in Hong Kong. Vaccine 2021;39(7):1148–56.
- [34] Hawkins RB, Charles E, Mehaffey JH. Socio-economic status and COVID-19– related cases and fatalities. Public Health 2020;189:129–34.
- [35] Alfageeh El, Alshareef N, Angawi K, Alhazmi F, Chirwa GC. Acceptability of a COVID-19 vaccine among the Saudi population. Vaccines 2021;9(3):226.