JIDC | THE JOURNAL OF INFECTION IN DEVELOPING COUNTRIES

Original Article

Vaccine hesitancy and refusal among parents: An international ID-IRI survey

Yakup Cag[1], Mohammad Emad al Madadha[2,3], Handan Ankarali[4], Yasemin Cag[5], Kubra Demir Onder[6], Aysegul Seremet-Keskin[6], Filiz Kizilates[6], Rok Čivljak[7], Ghaydaa Shehata[8], Handan Alay[9], Sevil Alkan-Ceviker[10], Fatma Yilmaz-Karadag[11], Meliha Cagla-Sonmezer[12], Manar Ezzelarab Ramadan[13], Dumitru Irina Magdelena[14], Ljiljana Betica Radic[15], Jurica Arapovic[16], Fatma Kesmez-Can[9], Nagwa Mostafa El-Sayed[17], Oladapo Babatunde Campbell[18], Gulden Eser-Karlidag[19], Reham Khedr[20], Mehmet Emirhan Isik[21], Michael Mihailov Petrov[22], Roxana Cernat[14], Umran Erturk[23], Yesim Uygun-Kizmaz[21], Eva Huljev[24], Fatma Amer[25], Mehmet Resat Ceylan[26], Andrea Marino[27], Gulnur Kul[28], Tuba Damar-Cakirca[29], Yara Mohsen Khalaf[30], Arzu Cennet Isik[31], Olumuyiwa Elijah Ariyo[32], Ismail Necati Hakyemez[33], Rezaul Karim Ripon[34], Abdorrahim Afkhamzadeh[35], Emine Kubra Dindar-Demiray[36], Osasona Oluwadamilola Gideon[37], Maya Belitova[38], Mustafa Altindis[39], Rehab El-Sokkary[25], Recep Tekin[40], Mohammed Ahmed Garout[41,42], Joanna Zajkowska[43], Farhan Fazal[44], Muhammed Bekcibasi[45], Mirsada Hukic[46,47], Summiya Nizamuddin[48], Serkan Surme[49], Ricardo Fernandez[50], Amani El-Kholy[51], Nasim Akhtar[52], Saadia Ijaz[53], Andrea Cortegiani[54,55], Meliha Meric-Koc[56], Hakan Hasman[57], Agah Victor Maduka[58], Jehan Ali ElKholy[59], Sema Sari[60], Mumtaz Ali Khan[61], Yasemin Akin[1], Sukran Kose[62], Hakan Erdem[63]

[1] Department of Pediatrics, University of Health Sciences Kartal Dr. Lutfi Kirdar City Hospital, Istanbul, Turkey
[2] Department of Microbiology and Immunology, Institute of Marine and Environmental Technology, University of Maryland School of Medicine, Baltimore, Maryland, United States
[3] Department of Pathology, Microbiology and Forensic Medicine, School of Medicine, The University of Jordan, Amman, Jordan
[4] Department of Biostatistics and Medical Informatics, Istanbul Medeniyet University Faculty of Medicine, Istanbul, Turkey
[5] Department of Infectious Diseases and Clinical Microbiology, Istanbul Medeniyet University Faculty of Medicine, Istanbul, Turkey
[6] Department of Infectious Diseases and Clinical Microbiology, University of Health Sciences Antalya Training and Research Hospital, Antalya, Turkey
[7] Department for Respiratory Tract Infections, Dr. Fran Mihaljević University Hospital for infectious Diseases, University of Zagreb School of Medicine, Zagreb, Croatia
[8] Department of Neurology, Assiut University Faculty of Medicine, Assiut, Egypt
[9] Department of Infectious Diseases and Clinical Microbiology, Ataturk University Faculty of Medicine, Erzurum, Turkey
[10] Department of Infectious Diseases and Clinical Microbiology, Onsekiz Mart University Faculty of Medicine, Canakkale, Turkey
[11] Department of Infectious Diseases and Clinical Microbiology, University of Health Sciences Sancaktepe Şehit Prof. Dr Ilhank Varank Training and Research Hospital, İstanbul, Turkey
[12] Department of Infectious Diseases and Clinical Microbiology, Hacettepe University Faculty of Medicine, Ankara, Turkey
[13] Department of Parasitology, Suez University Faculty of Medicine, Egypt
[14] Department of Infectious Diseases, Clinical Infectious Diseases Hospital Constanta, Ovidius University of Constanta, Constanta, Romania
[15] Department of Infectious Diseases, General Hospital Dubrovnik, Dubrovnik, Croatia
[16] Department of Infectious Diseases, University Clinical Hospital Mostar, Mostar, Bosnia and Herzegovina
[17] Department of Medical Parasitology, Research Institute of Ophthalmology, Giza, Egypt
[18] Department of Infectious Diseases, Grace Hospital, Lagos, Nigeria
[19] Department of Infectious Diseases and Clinical Microbiology, University of Health Sciences Fethi Sekin City Hospital, Elazig, Turkey
[20] Department of Pediatric Oncology, National Cancer Institute - Cairo University / Children Cancer Hospital Egypt, Cairo, Egypt
[21] Department of Infectious Diseases and Clinical Microbiology, University of Health Sciences Kosuyolu Training and Research Hospital, Istanbul, Turkey
[22] Department of Microbiology and Immunology, Medical University of Plovdiv Faculty of Pharmacy, Plovdiv, Bulgaria
[23] Department of Infectious Diseases, Bahrain Oncology Center, Bahrain
[24] Department for Respiratory Tract Infections, Dr. Fran Mihaljević University Hospital for Infectious Diseases, Zagreb, Croatia
[25] Department of Medical Microbiology and Immunology, Faculty of Medicine, Zagazig University, Zagazig, Egypt
[26] Department of Infectious Diseases and Clinical Microbiology, MD. University of Harran Faculty of Medicine, Şanliurfa, Turkey
[27] Department of Clinical and Experimental Medicine, ARNAS Garibaldi Unit of Infectious diseases, University of Catania, Catania, Italy
[28] Department of Infectious Diseases and Clinical Microbiology, Kirikhan state Hospital, Hatay, Turkey
[29] Department of Infectious Diseases and Clinical Microbiology, Şanliurfa training and research hospital, Sanliurfa, Turkey
[30] Department of epidemiology High institute of public health,Alexandria University Infectious Disease Clinical pharmacist, Antimicrobial stewardship department, International Medical Center Hospital, Alexandria, Egypt

[31] Department of Internal Medicine, University of Health Sciences Kartal Dr. Lutfi Kirdar City Hospital, Istanbul, Turkey
[32] Department of Infectious Diseases and Tropical Medicine, Federal Teaching Hospital Ido-Ekiti, Ekiti, Nigeria
[33] Department of Infectious Diseases and Clinical Microbiology, Balikesir University Faculty of Medicine, Balikesir, Turkey
[34] Department of Public Health and Informatics, Jahangirnagar University, Savar, Bangladesh
[35] Department of Community Medicine, Kurdistan University of Medical Sciences, Sanandaj, Iran
[36] Department of Infectious Diseases and Clinical Microbiology, Bitlis State Hospital, Bitlis, Turkey
[37] Department of Medical Services, Hospitals Management Board, Ekiti State, Nigeria
[38] Department of Anesthesiology and Intensive Care, University Hospital "Queen Giovanna"-ISUL, EAD, Sofia, Bulgaria
[39] Department of Microbiology, Sakarya University Faculty of Medicine, Sakarya, Turkey
[40] Department of Infectious Diseases and Clinical Microbiology, Dicle University Faculty of Medicine, Diyarbakir, Turkey
[41] Department of Community Medicine and Health Care for Pilgrims, Umm Al-Qura University Faculty of Medicine, Makkah, Saudi Arabia
[42] Department of Infection Control, Saudi German Hospital, Jeddah, Saudi Arabia
[43] Department of Infectious Diseases and Neuroinfections, Medical University in Białystok, Bialystok, Poland
[44] Department of Medicine, Kasturba Medical College Mangalore, Mangalore, India
[45] Department of Infectious Diseases and Clinical Microbiology, Bismil State Hospital, Diyarbakir, Turkey
[46] Department of Clinical Microbiology, Institute for Biomedical Diagnostic and Research NALAZ, Sarajevo, Bosnia and Herzegovina
[47] Department for Medical Sciences, Academy of Science and Arts of Bosnia and Herzegovina, Sarajevo, Bosnia and Herzegovina
[48] Section of Microbiology, Department of Pathology, Shaukat Khanum Memorial Cancer Hospital and Research Centre, Lahore, Pakistan
[49] Department of Infectious Diseases and Clinical Microbiology, University of Health Sciences Haseki Training and Research Hospital, Istanbul, Turkey
[50] Department of Pulmonary and Critical Care, San Juan City Hospital, San Juan, Puerto Rico
[51] Department of Clinical Pathology, Cairo University Hospital, Cairo, Egypt
[52] Department of Infectious Diseases, Pakistan Institute of Medical Sciences, Islamabad, Pakistan
[53] Department of Pathology, Shalamar institute of health sciences, Lahore, Pakistan
[54] Department of Surgical, Oncological and Oral Science (Di.Chir.On.S.), University of Palermo, Palermo, Italy
[55] Department of Anesthesia, Intensive Care and Emergency, Policlinico Paolo Giaccone, Palermo, Italy
[56] Department of Infectious Diseases and Clinical Microbiology, Bezmialem Vakif University Faculty of Medicine, Istanbul, Turkey
[57] Department of Emergency, Ankara Medicalpark Private Hospital, Ankara, Turkey
[58] Department of Microbiology, Ebonyi State University Teaching Hospital Abakaliki, Ebonyi State, Nigeria
[59] Department of Anesthesia, Pain Management, Cairo University Hospital, Cairo, Egypt
[60] Department of Intensive Care, Nigde Training and Research Hospital, Nigde, Turkey
[61] Department of Epidemiology and Disease Surveillance, National institute of health Islamabad, Islamabad, Pakistan
[62] Department of Infectious Diseases and Clinical Microbiology, Tepecik Training and Research Hospital, Izmir, Turkey
[63] ID-IRI Lead Coordinator, Ankara, Turkey

Abstract

Introduction: Although vaccines are the safest and most effective means to prevent and control infectious diseases, the increasing rate of vaccine hesitancy and refusal (VHR) has become a worldwide concern. We aimed to find opinions of parents on vaccinating their children and contribute to available literature in order to support the fight against vaccine refusal by investigating the reasons for VHR on a global scale.

Methodology: In this international cross-sectional multicenter study conducted by the Infectious Diseases International Research Initiative (ID-IRI), a questionnaire consisting of 20 questions was used to determine parents' attitudes towards vaccination of their children.

Results: Four thousand and twenty-nine (4,029) parents were included in the study and 2,863 (78.1%) were females. The overall VHR rate of the parents was found to be 13.7%. Nineteen-point three percent (19.3%) of the parents did not fully comply with the vaccination programs. The VHR rate was higher in high-income (HI) countries. Our study has shown that parents with disabled children and immunocompromised children, with low education levels, and those who use social media networks as sources of information for childhood immunizations had higher VHR rates ($p < 0.05$ for all).

Conclusions: Seemingly all factors leading to VHR are related to training of the community and the sources of training. Thus, it is necessary to develop strategies at a global level and provide reliable knowledge to combat VHR.

Key words: Vaccine hesitancy; vaccine refusal; parents.

J Infect Dev Ctries 2022; 16(6):1081-1088. doi:10.3855/jidc.16085

(Received 16 November 2021 – Accepted 22 February 2022)

Introduction

Vaccines contribute greatly to the prevention and control of infectious diseases [1]. Once vaccinated, an individual helps in protecting society from communicable diseases by preventing transmission in addition to the individual's protection [2]. It is estimated that vaccines prevent 2–3 million deaths each year [3]. Globally, vaccination programs have helped completely eradicate smallpox and successfully control infectious diseases, polio and measles in particular [4].

Although vaccines are the safest and most effective means available to prevent and control infectious diseases, the increasing rate of vaccine refusal has become a threat to public health worldwide [5]. The inadequate vaccination rates in the community could be attributed to the fact that parents refuse or delay the vaccination doses of their children [6]. Seemingly, increasing numbers of parents have doubts about the safety and necessity of vaccines and distrust in pharmaceutical industries [7].

In this study, we aimed to find the opinions of parents on vaccinating their children and contribute to the available literature to support the fight against vaccine hesitancy and refusal (VHR) by investigating the reasons on a global scale.

Methodology

Ethics committee approval dated 01.27.2021 and numbered 514/194/3 was obtained from the ethics committee of University of Health Sciences, Kartal Dr. Lütfi Kırdar City Hospital in Istanbul, Turkey for this international and cross-sectional multicenter survey. The study was conducted in accordance with the ethical principles of the Declaration of Helsinki.

Participating researchers/centers

Physicians from 16 countries (Bangladesh, Egypt, India, Nigeria, Pakistan, Turkey, Jordan, Bulgaria, Iran, Bosnia and Herzegovina, Italy, Croatia, Puerto Rico, Romania, Saudi Arabia, and Poland) participated in our study. They were contacted through the Infectious Diseases International Research Initiative (ID-IRI), which is an international clinical research platform. In minimizing the selection bias for the participating countries, we used cluster sampling method for the selection of the hospitals our researchers are working in. Each hospital itself is a mini representation of the other hospitals in their country. In addition, we did not provide comparisons based on the countries of the researchers in our study. Rather, we stratified the countries according to their economical statuses.

Data Collection

A questionnaire consisting of 20 questions was prepared to investigate the parents' demographic data such as country of residence, age, gender, education level (None, Primary school, High school, University, Master/Doctorate), occupation, whether they have a child with a chronic disease, whether they have a disabled child, as well as their views on childhood vaccines, their reasons for vaccine refusal or hesitation if they had any, and whether they comply with the vaccination programs in their own countries (see Supplementary-1). The questionnaire was pretested to minimize the chance of misinterpreting questions. The questionnaire was sent to the participants online via Google Drive between 1st March and 1st April 2021 and was administered face-to-face to a total of 4,029 parents (aged 18-63 years) with children aged < 13 years after obtaining their verbal consent. The participants have performed the survey through face-to-face interviews and submitted them via Google Drive.

Classifying parents/respondents

The parents were asked to choose one of the following responses to the statement "We should make childhood vaccinations to protect our children from infectious diseases": "1. Strongly disagree, 2. Disagree, 3. Undecided, 4. Agree, or 5. Strongly agree". Among these options, "Agree" or "Strongly agree" were considered vaccine approval, "Strongly disagree" or "Disagree" were considered vaccine refusal, and "Undecided" was considered vaccine hesitancy.

Economic concerns

The countries where the study was conducted were examined under 3 groups according to their economic development levels as follows: lower-middle-income (LMI) countries (Bangladesh, Egypt, India, Nigeria, and Pakistan), upper-middle-income countries (Turkey, Jordan, Bulgaria, Iran, and Bosnia, and Herzegovina), and high-income (HI) countries (Italy, Croatia, Puerto Rico, Romania, Saudi Arabia, and Poland) [8].

Statistical analysis

Descriptive statistics of the answers given to the questions in the survey were calculated as Mean, Standard Deviation (SD), count, and percentage frequencies. The relations between the answers given to the first 14 questions and the answers to the questions 15-21 were evaluated with Pearson chi-square analysis or Fisher-Freeman-Halton exact test. The statistical significance level was accepted as $p < 0.05$. The relationship between VHR and parameters like age,

gender, education level, occupation, whether their child has a chronic disease and/or disability, economic development levels of countries, and sources of information on vaccines was statistically investigated.

Results

Four thousand and twenty-nine parents were included in the study, and 2,863 (78.1%) among them were females. Their mean age was 37.1 ± 7.0 years (range, 18–63 years), and the mean age of the youngest children of the parents included was 5.2 ± 3.7 years (range, 0.10–13 years). In addition, the mean number of children of parents was 2.1 ± 1.1 children (range, 0–10 children).

Table 1. Sociodemographic characteristics of parents.

Parents	N (%)
Country	
Bangladesh	52 (1.3)
Bosnia and Herzegovina	120 (3.0)
Bulgaria	119 (3.0)
Croatia	299 (7.4)
Egypt	567 (14.1)
India	46 (1.1)
Iran	53 (1.3)
Italy	77 (1.9)
Jordan	299 (7.4)
Nigeria	195 (4.8)
Pakistan	125 (3.1)
Poland	49 (1.2)
Puerto Rico	32 (0.8)
Romania	160 (4.0)
Saudi Arabia	48 (1.2)
Turkey	1788 (44.4)
Country's income level	
Low Middle	985 (24.4)
Upper Middle	2379 (59.0)
High	665 (16.5)
Gender	
Female	2863 (71.1)
Male	1166 (28.9)
Occupation	
Housewife	844 (20.9)
Worker	1197 (29.7)
Civil servant	1088 (27.0)
Free occupation	554 (13.8)
*Health care worker	346 (8.6)
Education status	
None	53 (1.3)
Primary school	365 (9.1)
High school	888 (22.0)
University	1792 (44.5)
Master/Doctorate	931 (23.1)
Have a child with a chronic illness	412 (10.2)
Have an immunocompromised child	147 (3.6)
Have a disabled child	204 (5.1)
Intellectual disability	82 (2.0)
Motor disability	64 (1.6)
Autistic disorder	47 (1.2)
Hearing loss	11 (0.3)
Visual disturbances and blindness	24 (0.6)
Language and speech disorder	5 (0.1)

* One who delivers care and services to the sick and ailing either directly as doctors and nurses or indirectly as aides, helpers, laboratory technicians, or even medical waste handlers.

Parental characteristics

The parent's education level, occupation, country, income level of their country, and status of having a disabled child, a child with a chronic disease, or an immunocompromised child of the parents included were given in Table 1.

Sources of information on childhood immunizations

Responses given to the multiple-choice question in the survey regarding the sources of information on childhood immunizations for the parents were as follows: from healthcare institutions, physicians, and other healthcare professionals (90.2%); from print, visual, and audio media (newspaper, magazine, TV, radio, etc.) (20.2%); from the internet and social media networks (20.2%); from their relatives and friends (18.2%); and other sources (0.6%) (Table 2).

Vaccine hesitancy and refusal rates

The number of parents in the vaccine approval group was 3,477 (86.3%), "undecided" (vaccine hesitancy) group was 314 (7.8%), and vaccine refusal group was 238 (5.9%) (Table 2). The overall vaccine hesitancy and refusal rate of the parents were found to be 13.7%. Reasons for vaccine refusal and vaccine hesitancy are presented in Figure 1, Figure 2, and Table 2.

Compliance with vaccination programs

We found that 3,283 (80.7%) parents had their children vaccinated completely and routinely, 495 (12.3%) had their children vaccinated completely but with some delays, 234 (5.8%) had their children vaccinated incompletely, and 47 (1.2) did not have their children vaccinated at all (Table 2). In total, 19.3% of the parents did not fully comply with the vaccination programs.

Parental VHR and its' relations

The highest VHR rate was detected in HI countries ($p < 0.005$). The lowest VHR rate was among healthcare workers and the highest VHR rate was among self-employed individuals ($p < 0.001$). The lowest VHR rate was found to be among university graduates and the highest VHR rate was among individuals with no education ($p < 0.001$).

Figure 1. The reasons for vaccine refusal.

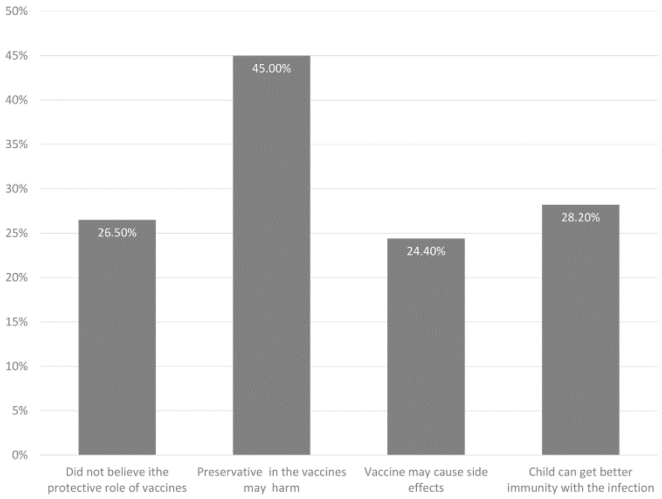

Figure 2. The reasons for vaccine hesitancy.

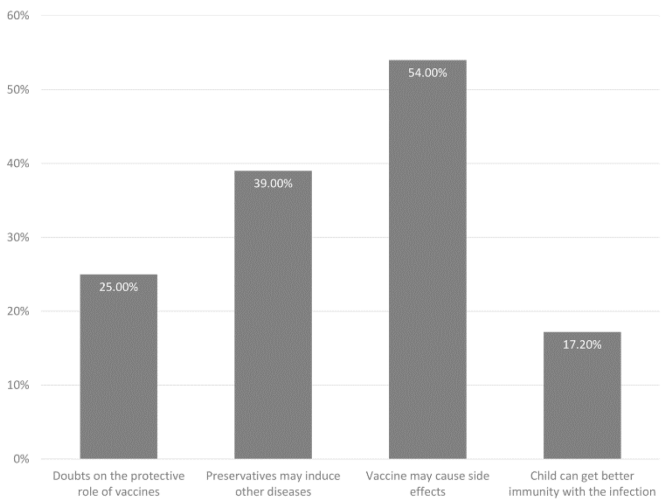

Table 2. Parents' responses to survey questions.

Survey questions directed to parents		**N (%)**
Who makes the decision about vaccination of your child?	Mother	850 (21.1)
	Father	305 (7.6)
	Joint decision of parents	2838 (70.4)
	*Other	36 (0.9)
Where do you get information about childhood vaccines?	From health care institutions, physicians and other health professionals	3636 (90.2)
	written, visual and audio media (Newspaper, Magazine, TV, Radio)	812 (20.2)
	Internet and social media networks	812 (20.2)
	The relatives and friends	735 (18.2)
	**Other	25 (0.6)
We need to make childhood vaccinations to protect our children from infectious diseases	Agree, strongly agree	3477 (86.3)
	Undecided	314 (7.8)
	Disagree, strongly disagree	238 (5.9)
"Disagree or strongly disagree" group	***Subtotal***	238 (5.9)
	I do not believe in the protective role of vaccines.	63 (1.6)
	Preservative substances in the vaccine may cause harm to my child.	107 (2.7)
	The vaccine may cause side effects in my child	58 (1.4)
	My child can gain better immunity through experiencing an illness	67 (1.7)
	Other	4 (0.1)
"Undecided" group	***Subtotal***	
	I have doubts about the protective role of vaccines.	78 (1.9)
	Preservative substances in the vaccine may cause harm to my child.	122 (3.0)
	The vaccine may cause side effects in my child	169 (4.2)
	My child can gain better immunity through experiencing an illness	54 (1.3)
	Other	1 (0.0)
Do you have your children regularly and fully vaccinated in accordance with the routine vaccination program in your country?	I have my children regularly and fully vaccinated	3253 (80.7)
	I have the vaccines fully done, but some delays may occur for various reasons	495 (12.3)
	Not on a regular basis. Some vaccines are missed	234 (5.8)
	I do not have my children vaccinated at all	47 (1.2)
If your answer is "Not on a regular basis. Some vaccines are missed". Specify the reason	***Subtotal***	234 (5.8)
	I forget the timing of some vaccinations	147 (3.6)
	I cannot afford time to go to a health facility.	93 (2.3)
	I do not want my child to be vaccinated with particular vaccines.	104 (2.6)
	Other	23 (0.6)
Do you think that other children who are not vaccinated may put your child at risk?	Agree, strongly agree	2629 (65.3)
	Undecided	732 (18.2)
	Disagree, strongly disagree	668 (16.6)

*Pediatrician, family doctor, grandmother, government; **Medical books, medical publication, medical sources.

The VHR rate was found to be higher in parents with disabled children ($p < 0.001$), among parents with children having hearing loss and visual disturbances and blindness ($p < 0.05$), and in parents with immunocompromised children ($p < 0.05$). VHR rate was found to be lowest for parents who made a joint decision whether to vaccinate their children and at the highest rate in cases where the father made the decision alone ($p < 0.001$). No statistically significant difference was found between VHR and gender and having a child with a chronic disease ($p > 0.05$) (Table 3).

VHR and sources of information for vaccination

VHR rate was lower in parents receiving information on childhood immunizations from healthcare institutions, physicians, and other healthcare professionals, whereas it was higher among those who responded to this question as "from print, visual, and audio media (newspaper, magazine, TV, or radio)," "from the internet and social media networks," and "from my relatives and friends" ($p < 0.001$) (Table 3).

Table 3. Relationship between parents' characteristics with VHR.

		Vaccine approval		Vaccine hesitancy and refusal		*p*
		n	%	n	%	
Country's income level	Low Middle	846 a, b	85.9	139 a, b	14.1	
	Upper Middle	2083 a	87.6	296 a	12.4	0.003
	High	548 b	82.4	117 b	17.6	
The gender of the respondent	Female	2484	86.8	379	13.2	0.181
	Male	993	85.2	173	14.8	
The occupation of the respondent (parent)	Housewife	714 a, c	84.6	130 a, c	15.4	
	Worker	1030 a, b	86.0	167 a, b	14.0	
	Civil servant	958 b	88.1	130 b	11.9	< 0.001
	Free occupation	455 c	82.1	99 c	17.9	
	Health care worker	320 d	92.5	26 d	7.5	
Education status of the respondent (parent)	None	30 a	56.6	23 a	43.4	
	Primary school	296 b	81.1	69 b	18.9	
	High school	729 b	82.1	159 b	17.9	< 0.001
	University	1601 c	89.3	191 c	10.7	
	Master / Doctorate	821 c	88.2	110 c	11.8	
Child with a chronic illness	Yes	344 a	83.5	68	16.5	0.081
	No	3133	86.6	484	13.4	
Immunocompromised child	Yes	117 a	79.6	30 a	20.4	0.016
	No	3360 b	86.6	522 b	13.4	
Disabled child	Yes	158 a	77.5	46 a	22.5	< 0.001
	No	3319 b	86.8	506 b	13.2	
Intellectual disability	Yes	65	79,3	17	20.7	0.061
	No	3412	86,4	535	13.6	
Motor disability	Yes	52	81.3	12	18.8	0.236
	No	3425	86.4	540	13.6	
Autistic disorder	Yes	37	78.7	10	21.3	0.129
	No	3440	86.4	542	13.6	
Hearing loss	Yes	4 a	36.4	7 a	63.6	< 0.001
	No	3473 b	86.4	545 b	13.6	
Visual disturbances and blindness	Yes	16 a	66.7	8 a	33.3	0.005
	No	3461 b	86.4	544 b	13.6	
Who makes the decision about vaccination of your child?	Mother	709 a	83.4	141 a	16.6	
	Father	235 b	77.0	70b	23.0	< 0.001
	Joint decision	2501 c	88.1	337 c	11.9	
	Other	32 a, b, c	88.9	4 a, b, c	11.1	
Information Source						
Health care institutions, physicians, health professionals	Yes	3218 a	88.5	418 a	11.5	< 0.001
	No	259 b	65.9	134 b	34.1	
Written, visual and audio media (Newspaper, Magazine, TV, Radio)	Yes	668 a	82.3	144 a	17.7	< 0.001
	No	2809 b	87.3	408 b	12.7	
Internet and social media networks	Yes	643 a	79.2	169 a	20.8	< 0.001
	No	2834 b	88.1	383 b	11.9	
Relatives and friends	Yes	596 a	81.1	139 a	18.9	< 0.001
	No	2881 b	87.5	413 b	12.5	

The letters next to the frequencies show the differences between the rows. A significantly different option of the question carries a different letter.

Discussion

Although vaccination is currently one of the most effective tools in protecting public health, parental doubts about the safety and necessity of vaccines are on the rise [7]. These concerns subsequently prevent or delay vaccination in children, thereby paving a path for preventable infectious diseases and epidemics [9]. Measles increased by 30% globally in 2018, with the highest rates having been found in Italy and Romania between 2017 and 2018 [10]. In our survey, we analyzed the reasons for VHR at the international level by the opinions of parents for vaccinating their children, and we found that VHR rate was 13.7%. It was observed that the likelihood of preservatives in the vaccine may cause adverse effects in their children, and this was the most common cause of VHR. We found that 19.3% of the parents did not fully comply with the vaccination programs. The highest VHR rate was found in HI countries in parents with low education levels, with disabled and immunocompromised children, and in parents deciding on vaccination of their children individually. In addition, we have observed that the VHR rate was higher among parents who used social media networks as sources of information for childhood immunizations.

Parental VHR rates may vary across societies, regions, and countries [11-15]. In our study, which included respondents from 16 countries, the VHR rates of countries were different from each other; the overall vaccine hesitancy rate was 7.8% and the overall vaccine refusal rate was 5.9%. Alternatively, as in this study, various studies have reported that individuals against vaccination were more common in HI countries [9,16,17]. In addition, the low education level of parents was reportedly associated with VHR confirming our results [11,15]. Unsurprisingly, VHR increased as the education level of parents with VHR decreased.

In addition to individual factors such as parents' knowledge, attitudes, and beliefs, other complex and multidimensional factors were already known to affect the decisions made by parents to have their children vaccinated [18]. Thus, precise communication is essential for vaccination programs to achieve success. Providing effective and transparent information to the public about vaccines and considering people's concerns about vaccines are essential elements for decision-makers related to vaccination [19]. Misinformation about the efficacy and safety of vaccines affects vaccination programs undesirably and leads to VHR. Thus, preventable diseases may re-emerge and turn into epidemics owing to the reduced vaccination rates. One of the relatively new examples is the vaccine-preventable outbreak in the former Soviet Union countries due to the break in the chain of vaccination between 1990 to 1995 [20,21]. Currently, it appears that the internet and social media are the most important communication tools for influencing the parents' attitudes of distrust and refusal of vaccines [10,22]. The anti-vaccination movement has been prevalent since the first vaccine was invented and is now stronger than ever because of the internet, which has the potential to reach and influence every single parent. We are reporting in this study, as in the previous studies, that parents with VHR used the internet and social media tools more commonly as a source of information about immunization [13,23,24].

The main factor influencing parental decisions on whether or not to vaccinate their children was reported to be the safety of vaccines [25]. Concerns about serious side effects of vaccines and their ingredients were reported to be among the most important reasons that led to parental VHR for childhood vaccines [2,12,15,26,27] and our data supported this inference. Although there is no direct relationship between vaccination and disability, VHR rates were found to be high in parents with disabled children in this study. The probable reason seems that parents with disabled children are already stunned by the misinformation against vaccination.

The World Health Organization (WHO) stated that the vaccination rates should be above 95% for particular vaccines such as measles, to provide herd immunity for protection against vaccine-preventable diseases [28]. Although in this international multicenter study, we found that the rate of full compliance with the vaccination programs recommended by the decision-makers was 80.7%, 1.2% chose not to have any vaccinations at all, and 5.8% had their children vaccinated incompletely. This result is below the WHO recommended threshold. This inadequate compliance may cause the re-emergence of epidemics and can put the whole world in danger as well.

The main limitation of this study was that the number of questionnaires was not homogeneously distributed in the participating countries. Nevertheless, the strengths of the study were that either there was participation from 16 different countries or the centers that can represent country averages were included in the survey. In addition, the fact that the number of men participating in this study was less than women may have partially affected the results.

In conclusion, the factors leading to VHR are seemingly related to training of the community and the sources of training. Unfortunately, the current level of

full compliance for vaccination is below the WHO target. It is crucial to develop strategies at the global level to combat VHR.

References

1. Doornekamp L, Van-Leeuwen L, Van-Gorp E, Voeten H, Goeijenbier M (2020) Determinants of vaccination uptake in risk populations: A comprehensive literature review. Vaccines 8: 480.
2. Wagner CE, Prentice JA, Saad-Roy CM, Yang L, Grenfell B, Levin SA, Laxminarayan R (2020) Economic and behavioral influencers of vaccination and antimicrobial use. Front Public Health 8:975.
3. Gualano MR, Olivero E, Voglino G, Corezzi M, Rossello P, Vicentini C, Bert F, Siliquini R (2019) Knowledge, attitudes and beliefs towards compulsory vaccination: A systematic review. Hum Vaccin Immunother 15: 918-931.
4. Greenwood B (2014) The contribution of vaccination to global health: past, present and future. Philos Trans R Soc Lond B: Biol Sci 369:1645.
5. Ten threats to global health in 2019. Available: https://www.who.int/news-room/spotlight/ten-threats-to-global-health-in-2019: Accessed: 26 January 2022.
6. Henrikson NB, Anderson ML, Opel DJ, Dunn J, Marcuse EK, Grossman DC (2017) Longitudinal trends in vaccine hesitancy in a cohort of mothers surveyed in Washington State, 2013-2015. Public Health Rep 132: 451-454.
7. Dempsey AF, Wagner N, Narwaney K, Pyrzanowski J, Kwan BM, Kraus C, Gleason K, Resnicow K, Sevick C, Cataldi J, Brewer SE, Glanz JM (2019) 'Reducing Delays In Vaccination' (REDIVAC) trial: A protocol for a randomised controlled trial of a web-based, individually tailored, educational intervention to improve timeliness of infant vaccination. BMJ open 9: e027968.
8. Updated country income classifications for the World Bank's 2020 fiscal year. Available: https://datahelpdesk.worldbank.org/knowledgebase/articles/906519-world-bank-country-and-lending-groups. Accessed: 10 June 2021.
9. Siddiqui M, Salmon DA, Omer SB (2013) Epidemiology of vaccine hesitancy in the United States. Hum Vaccin Immunother 9: 2643-2648.
10. Carrieri V, Madio L, Principe F (2019) Vaccine hesitancy and (fake) news: Quasi-experimental evidence from Italy. Health economics 28: 1377-1382.
11. Bertoncello C, Ferro A, Fonzo M, Zanovello S, Napoletano G, Russo F, Baldo V, Cocchio S (2020) Socioeconomic determinants in vaccine hesitancy and vaccine refusal in Italy. Vaccines 8: 276.
12. Alsuwaidi AR, Elbarazi I, Al-Hamad S, Aldhaheri R, Sheek-Hussein M, Narchi H (2020) Vaccine hesitancy and its determinants among Arab parents: a cross-sectional survey in the United Arab Emirates. Hum Vaccin Immunother 16: 3163-3169.
13. Çağ Y (2020) Parental attitudes toward vaccination in Turkey: a face-to-face survey. J Pediatr Infect Dis 15: 184-188.
14. Kalok A, Loh SYE, Chew KT, Aziz NHA, Shah SA, Ahmad S, Ismail NAM, Mahdy ZA (2020) Vaccine hesitancy towards childhood immunisation amongst urban pregnant mothers in Malaysia. Vaccine 38: 2183-2189.
15. Kempe A, Saville AW, Albertin C, Zimet G, Breck A, Helmkamp L, Vangala S, Dickinson M, Rand C, Humiston S, Szilagyi PG (2020) Parental hesitancy about routine childhood and influenza vaccinations: a national survey. Pediatrics 146: e20193852
16. Wei F, Mullooly JP, Goodman M, McCarty MC, Hanson AM, Crane B, Nordin JD (2009) Identification and characteristics of vaccine refusers. BMC pediatrics 9: 1-9.
17. Sanou A, Simboro S, Kouyaté B, Dugas M, Graham J, Bibeau G (2009) Assessment of factors associated with complete immunization coverage in children aged 12-23 months: a cross-sectional study in Nouna district, Burkina Faso. BMC Int Health Hum Rights 9: 1-15.
18. Dubé E, Vivion M, MacDonald NE (2015) Vaccine hesitancy, vaccine refusal and the anti-vaccine movement: influence, impact and implications. Expert Rev. Vaccines 14: 99-117.
19. Bozzola E, Spina G, Tozzi AE, Villani A (2020) Global measles epidemic risk: current perspectives on the growing need for implementing digital communication strategies. Risk Manag Healthc Policy 13: 2819-2826.
20. Hardy IR, Sutter RW, Dittmann S (1996) Current situation and control strategies for resurgence of diphtheria in newly independent states of the former Soviet Union. The Lancet 347: 1739-1744.
21. Nağıyev A, Erdem H, Eyigün CP, Pasha A (2004) Erişkinlerde gözlenen 51 difteri olgusunun irdelenmesi. Klimik 10: 196-199.
22. Tafuri S, Gallone MS, Cappelli MG, Martinelli D, Prato R, Germinario C (2014) Addressing the anti-vaccination movement and the role of HCWs. Vaccine 32: 4860-4865.
23. Gianfredi V, Moretti M, Lopalco PL (2019) Countering vaccine hesitancy through immunization information systems, a narrative review. Hum Vaccines Immunother 15: 2508-2526.
24. Chiou L, Tucker C (2018) Fake News and Advertising on Social Media. Available: https://www.nber.org/system/files/working_papers/w25223/w25223.pdf: Accessed : 21 May 2021.
25. Salmon DA, Moulton LH, Omer SB, deHart MP, Stokley S, Halsey NA (2005) Factors associated with refusal of childhood vaccines among parents of school-aged children: A case-control study. Arch Pediatr Adolesc Med 159: 470-476.
26. Smith TC (2017) Vaccine rejection and hesitancy: A review and call to action. Open Forum Infect Dis 4:1-7.
27. Hough-Telford C, Kimberlin DW, Aban I, Hitchcock WP, Almquist J, Kratz R, O'Connor KG (2016) Vaccine delays, refusals, and patient dismissals: a survey of pediatricians. Pediatrics 138: e20162127.
28. World Health Organization (WHO) Europe (2013) The Guide to Tailoring Immunization Programmes (TIP) and child vaccination in the 2013 Available: https://www.euro.who.int/__data/assets/pdf_file/0003/187347/The-Guide-to-Tailoring-Immunization-Programmes-TIP.pdf. Accessed: 21 May 2021.

Corresponding author

Yakup Cag, Assoc. Prof, MD
Department of Pediatrics, University of Health Sciences,
Kartal Dr. Lütfi Kırdar City Hospital,
Kartal/Istanbul, Turkey
Phone: +90 216 4413900
E-mail: yakupcag@hotmail.com

Conflict of interests: No conflict of interests is declared.