Evaluation of Immunization Status in Patients with Cerebral Palsy: Multicenter CP-VACC Study

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Abstract

Children with chronic neurological diseases,including cerebral palsy(CP)are especially susceptible to vaccine-preventable infections and face an increased risk of severe respiratory infections and decompensation of their disease.This study aims to examine age-appropriate immunization status and related factors in the CP population of our country.

This cross-sectional prospective multicentered survey study included 18 pediatric neurology clinics around Turkey,wherein outpatients children with CP were included in the study.Data on patient and CP characteristics,concomitant disorders as well as vaccination status included in the National Immunization Program(NIP),administration and recommendation of influenza vaccine were collected at a single visit.

A total of 1194 patients were enrolled.Regarding immunization records,the most frequently administrated and schedule completed vaccines were BCG(90.8%),hepatitis B(88.9%)and oral poliovirus vaccine (88.5%).MMR was administered to 77.3% and DTaP-IPV-HiB was administered to 60.5% of patients.For the pneumococcal vaccines,54.1% of children had received PCV in the scope of the NIP, and 15.2% of children were not fully vaccinated for their age.The influenza vaccine, was administered only to 3.4% of the patients at any time and had never been recommended to 1122 parents(93.9%).In the patients with severe(grade 4 and 5)motor dysfunction,the frequency of incomplete/none vaccination of hepatitis B,BCG, DTaP-IPV-HiB,OPV,MMR were statistically more common than mild to moderate(grade 1–3)motor dysfunction($p = 0.003$, $p < 0.001$, $p < 0.001$, $p < 0.00$, and $p < 0.001$, respectively).Influenza vaccine recommendation by physicians was higher in the severe motor dysfunction group and the difference was statistically significant($p = 0.029$).

Children with CP had lower immunization rates and incomplete immunization programs.Clinicians must ensure children with CP receive the same preventative health measures as healthy children,including vaccines.

Introduction

Cerebral palsy (CP) is the most common chronic neurological disorder and the most common cause of physical disability in childhood. Patients have decreased muscle tone, weakness, inability to handle the secretions, and impairment of pulmonary functions. Children with neurological disorders have a 5–7 times higher risk of hospitalization due to respiratory diseases among all children (1). Recurrent respiratory infections are one of the most important causes of morbidity and mortality for these patients. Like in healthy children, routine immunization is one of the most important preventive measures for infectious disease among children with chronic neurological diseases, including CP. Health authorities have defined chronic neurological diseases as high-risk conditions for influenza and pneumococcal infections, and they recommend vaccines against these infections (2). Although children with chronic diseases face greater risks, their vaccine coverage rates appear to be lower than in the general population

(3); nonetheless, exact figures are unavailable. In previous studies, it was revealed that patients with chronic neurological diseases were vaccinated more delayed and less frequently than the healthy population (1, 4, 5).

Today, an up-to-date vaccination schedule is established in Turkey with the gradual development of new vaccines, strains, and application methods. Turkey's National Immunization Program (NIP) is effective against 13 different antigens (tetanus, diphtheria, pertussis, polio, Hemophilus influenza type B, hepatitis B, tuberculosis, mumps, measles, rubella, pneumococcus, hepatitis A, varicella). There are only a few studies in Turkey that determine the immunization status of children with chronic illnesses especially chronic neurologic diseases (5). Immunization in these children is particularly important as they often have underlying chronic illnesses that result in a significantly higher risk of complications from infectious diseases that are vaccine-preventable (e.g. influenza and invasive pneumococcal disease).

There are many misconceptions about the adverse reactions to vaccines. In truth, vaccinations may elicit serious adverse reactions, such as anaphylaxis, which is a very rare occurrence (6). Often there are myths to dispel, such as fears about the overload of the immune system, to do more injections in the same session, excessive reactogenicity, and some false contraindications.

Parents of patients with CP may also have prejudices about the vaccines, as epilepsy usually accompanies the clinical picture.
Also, given the multiple health-care providers involved in children with disabilities, no particular clinicians may take on the role of ensuring preventative health measures are addressed.

The main objective of the present study is to examine vaccination rates in the CP population of our country. The secondary objective is to explore whether there is an association between demographic, medical, and receipt of the vaccines which are included in NIP. We hypothesized that patients with CP receive the vaccinations less frequently than the healthy population.

Methods

Study Protocol

In August 2018, a questionnaire form including demographic and clinical features, vaccination status of patients with CP, and the vaccination recommendation of clinicians was prepared at the Izmir Tepecik Training and Research Hospital Pediatric Infection Diseases and İzmir Katip Celebi University Pediatric Neurology Clinics. In September 2018, we contacted the hospitals via e-mails requesting that the questionnaire be completed by a pediatric neurologist from each center. Detailed information about the study was given to the clinics that accepted to participate in the study. Pediatric neurologists were asked to fill in the questionnaire forms by obtaining an informed consent form from the parents/legal guardians of the patients. Printed questionnaires were sent to centers that agreed to participate in the study and data were collected from September 2018 to February 2019.

Data Sources

Data on patient demographics (age, gender), CP characteristics [etiology and type of CP, affected body parts, GMFCS (Gross Motor Function Classification System) level], concomitant nonneuromotor impairments, hospitalization in the last year, number of hospitalizations and reasons, medicines used regularly, vaccination status for each antigen (included and non-included in NIP), recommended influenza vaccine from clinicians were collected at a single visit. The evaluation of the immunization rate in the population included immunization cards/records provided by parents. We defined “complete” or “incomplete” vaccinations, considering whether the vaccine was available in the NIP during the children’s immunization period.

CP was clinically categorized into spastic, dyskinetic or extrapyramidal, cerebellar or ataxic, hypotonic, and mixed, based on the predominant motor impairment (7). GMFCS was used to classify the severity of motor impairment into five subgroups including level I (walks without limitations), level II (walks with limitations), level III (walks using a hand-held mobility device), level IV (self-mobility with limitations, may use powered mobility) and level V (transported in a manual wheelchair) according to published criteria (8).

Study Population

Patients diagnosed with CP and ages under 18 years were included in the study. Of 1202 patients initially enrolled from 18 centers, 1194 patients were found eligible to participate in this study since 8 patients were excluded due to detection of protocol violation (all vaccine data were missing) after enrollment.

Written informed consent/assent was obtained from children and/or children's parents or legal guardian following a detailed explanation of the objectives and protocol.
The study was conducted following the ethical principles stated in the “Declaration of Helsinki” and approved by the institutional ethics committees (number: 21.02.2018/92).

Statistical Analysis

The obtained questionnaires were transferred to IBM SPSS (Windows, Version 23.0, Armonk, NY: IBM Corp) program on the computer. The suitability of the variables to normal distribution was examined by visual (histogram and probability plots (PP Plot)) and analytical methods (Kolmogorov-Smirnov test for $n > 50$) Descriptive data were given as mean and standard deviation for continuous variables and median (minimum-maximum values) for categorical variables. The parameters with normal distribution were compared by independent samples *t*-test in independent groups and non-normally parameters were compared with the *Mann-Whitney U test.* Comparisons for categorical variables were made using the Pearson chi-square test and Fischer’s exact test in 2x2 order. In the study, the significance of the p-value was considered as < 0.05.

Results

Questionnaires were obtained from 1202 patients and 8 patients were excluded due to significant missing data. Overall, 1194 children (57.7% boys and 42.3% girls) with CP and ages between 8 months to 18 years from 18 Pediatric Neurology Clinics. The number of patients according to centers was shown in Fig. 1. The mean age of patients was 93.9 ± 57.6 months (IQR; 44–135 months). The main etiology of CP were asphyxia (39.7%) and prematurity (39.6%), most of the patients had level V gross motor dysfunction (42.1%). Spastic CP (83.4%) with quadriplegic (29.2.0%) or hemiplegic (17.3%) topography was the most common type. The etiology and characteristics of CP have been summarized in Table 1. The most common concomitant diseases were epilepsy (56.2%), orthopedic problems (15.2%), and growth retardation (29.1%). Most of the patients were using medications (63.9%), the most frequently used drugs were antiepileptics (44.2%), and muscle relaxants (6.8%). Among patients with CP, 342 (28.6%) of them were hospitalized in the last year, of whom 178 were hospitalized due to pneumonia (Table 2).

Table 1
Etiology and characteristics of cerebral palsy

Etiology*	**n**	**%**
Asphyxia	474	39.7
Prematurity	473	39.6
Structural abnormalities	81	6.8
Intracranial hemorrhage	76	6.4
Metabolic encephalopathy	58	4.9
Multiple births	53	4.4
Meningitis encephalitis sequela	38	3.2
Head injury	22	1.8
Intrauterine infections	13	1.1
Others	18	1.5
Unknown origin	96	8.0
Clinical category		
Spastic	996	83.4
Atonic	54	4.5
Dyskinetic	40	3.4
Mixed	56	4.7
Missing data	48	4.0
Topography		
Quadriplegic	349	29.2
Hemiplegic	206	17.3
Paraplegic	138	11.6
Diplegic	84	7.0
Monoplegic	6	0.5
Missing data	411	35
Gross motor dysfunction		
Level 5	503	42.1
*Some patients may have more than one cause		

Etiology*	n	%
Level 4	140	11.7
Level 3	184	15.4
Level 2	181	15.2
Level 1	115	9.6
Missing data	71	5.9
*Some patients may have more than one cause		

Table 2
Demographical and clinical characteristics of patients with CP

Characteristics	
Age[a]	93.9 ± 57.6
Gender (male)[b]	689 (57.7)
Concomitant diseases[b]	959 (80.3)
epilepsy	671 (56.2)
orthopedic problems	500 (41.9)
growth retardation	348 (29.1)
visual disorders	182 (15.2)
recurrent pneumonia	116 (9.7)
auditory disorders	33 (2.8)
Using medications[b]	763 (63.9)
antiepileptics	528 (44.2)
antiepileptics + muscle relaxants	105 (8.8)
muscle relaxants	81 (6.8)
antipsychotics	13 (1.1)
antiepileptics + antipsychotics	11 (0.9)
muscle relaxants + antipsychotics	4 (0.3)
antiepileptics + muscle relaxants + antipsychotics	2 (0.2)
others	19 (1.6)
Hospitalization in the last year[b]	342 (28.6)
Hospitalization in the last year due to pneumonia[b]	178 (14.9)
[a] Values were given as mean ± SD, [b]Values were give as percentage	

Regarding immunization records, the most frequently administrated and schedule completed vaccines were Bacillus Calmette-Guerin (BCG) (n = 1084, 90.8%), hepatitis B (n = 1062, 88.9%), and oral poliovirus vaccine (n = 1057, 88.5%). Measles-mumps-rubella (MMR) were administered to 77.3% (n = 923) of patients and Diphtheria-Tetanus-acellular Pertussis-Inactivated Polio vaccine-Haemophilus influenzae type B (DTaP-IPV-HiB) were administered to 60.5% (n = 722) of patients (Table 3). In Turkey, conjugated

pneumococcal vaccine-7 (PCV7) was introduced to the NIP in April 2008 and was switched to PCV13 in November 2011. Before 2008, PCV requires a specific recommendation for patients. In our study population, 30.8% (n = 367) of the study group had not been previously vaccinated with PCV. For the pneumococcal vaccines, 646 children (54.1%) had received PCV in the scope of the NIP, and 181 children (15.2%) were not fully vaccinated for their age. The varicella vaccine, which was included to NIP in 2012 and started to be administered in 2013, was not administered to 611 children (54.4%). Similarly, the hepatitis A vaccine, which was included in the NIP in 2012, was not administered to 650 children (54.4%). Age-appropriate vaccination according to the NIP were depicted in Table 3. The influenza vaccine, which is still not included in our NIP, was administered only to 3.4% of the patients at any time. There were only 27 (2.3%) patients who received the influenza vaccine during the season of the study. Influenza vaccine had never been recommended to 1122 parents (93.9%).

Table 3
Age-appropriate vaccination according to the National Immunization programme

Vaccines	Completed	Incomplete	None
Hepatitis B	1062 (88.9)	41 (3.4)	91 (7.6)
BCG[a]	1084 (90.8)	-	110 89.2)
DTaP-IPV-Hib[b]	722 (60.5)	379 (31.7)	93 (7.8)
OPV[c]	1057 (88.5)	26 (2.2)	111 (9.3)
Pneumococcus	646 (54.1)	181 (15.2)	367 (30.8)
MMR[d]	923 (77.3)	111 (9.3)	160 (13.4)
Varicella	583 (48.8)	-	611 (51.1)
Hepatitis A	492 (41.2)	52 (4.4)	650 (54.4)

[a]Bacillus Calmette-Guerin, [b]Diphtheria, Tetanus, acellular Pertussis - Inactivated Polio vaccine - Haemophilus influenzae type B, [c]oral polio vaccine, [d]measles-mumps-rubella

Considering the administration rates of vaccines not included in the NIP, the rotavirus vaccine was administered to 4.8% (n = 58) and the meningococcal vaccine to 3.2% (n = 39) of the patients. None of the children with CP received the human papillomavirus vaccine.

In Turkey, MMR and DTaP-IPV were administered to children in the first grade of primary school. Among the reported reasons, the most important one for incomplete vaccination was the lack of primary school vaccination in our study population. Less reported reasons were parents thought that their children's' immune system was not strong enough to handle the vaccines, the cause of CP was due to vaccines, ACTH or IVIG therapy as it affects vaccination.

In the patients with severe (grade 4 and 5) motor dysfunction, the frequency of incomplete/none vaccination of hepatitis B, BCG, DTaP-IPV-HiB, OPV, MMR were statistically more common than mild to moderate (grade 1–3) motor dysfunction ($p = 0.003$, $p < 0.001$, $p < 0.001$, $p < 0.00$, and $p < 0.001$, respectively). Influenza vaccine recommendation by physicians was higher (in the severe motor dysfunction group and the difference was statistically significant ($p = 0.029$). Administration of influenza vaccine at any time or during the study period was also higher in patients with severe dysfunction but the differences were not statistically significant ($p = 0.313$, and $p = 0.163$). There was no statistical significance between severe and mild to moderate motor dysfunction in terms of pneumococcal vaccine administration ($p = 0.470$)

It was noted that BCG, OPV, MMR, and PCV vaccines were administered statistically more frequently in hospitalized patients with pneumonia in the last year ($p < 0.001$, $p < 0.001$, $p < 0.001$, and $p = 0.004$, respectively). And also, influenza vaccine recommendation, getting an influenza vaccine at any time and during the season of the study were statistically more common in this group ($p < 0.001$, $p = 0.034$, and $p = 0.022$, respectively).

Discussion

Our study aimed to explore immunization status in CP patients and examine whether there is an association between demographic, medical, and receipt of the vaccines which are included in NIP. To the best of our knowledge, the present multicenter study is the first in the English literature to investigate the immunization status of the CP population. Our results showed that the vaccination rate of children with CP for vaccines included in the Ministry of Health's NIP was lower than healthy children. These findings are similar to a Canadian study (9) that examined vaccination status in children with physical disabilities and included 57 children with CP. Their results showed lower than expected rates of vaccination (63%). The study results from Australia were found more remarkable, and the 'up-to-date' vaccination rate was demonstrated to be 19.2% in CP patients (10). In contrast, a study from Turkey (5), showed no significant difference between immunization rates of children with chronic neurologic diseases versus the healthy population. This study put forth the vaccination rate in 95.6% of patients with chronic neurologic diseases received age-appropriate vaccination according to the Ministry of Health's NIP. In our study, it was noticed that the administration rates were higher in vaccines that were included in the NIP previously (e.g., hepatitis B, BCG, OPV, MMR, DTaP-IPV-Hib), and lower in those added lastly (e.g., PCV, varicella, hepatitis A). This was attributed to the fact that nearly half of the patients presented in our study were born before vaccines were included in the NIP. MMR and DTaP-IPV-Hib vaccines, which are the other components of childhood vaccinations, have been found less completed with a rate of 77.3% and 60.5% respectively in this group than the vaccines included in the NIS for a long time. Similarly, Greenwood et al. evaluated the vaccination status of patients with CP, and the MMR vaccine was reported to be the most missed vaccine followed by DTaP -Hib, and OPV (10).

The patients with CP have a higher risk of morbidity and mortality than the healthy population for vaccine-preventable diseases. Respiratory diseases are the most frequently reported cause of morbidity

and mortality in CP, hence, by ameliorating respiratory status, quality of life, and life expectancy might be augmented. All studies of CP mortality investigating cause attribute more than half of the observed deaths to respiratory diseases (11). It is important to implement pneumococcal and influenza vaccines that cause pneumonia not to aggravate respiratory problems, which are the cause of almost half of the deaths. As with typically developing children, children with CP should be vaccinated per the currently used vaccination schedule. The rate of complete vaccination with PCV, which is recommended for all Turkish children, was lower in our study than in the general population, among which it is reported to exceed 95% after 2008 (12). Because of the recent implementation of the PCV, most of the older children born in Turkey before 2008 had not received it as a generally administered vaccine-like our patients. The most common cause associated with required hospitalization was pneumonia, with a rate of 52%, in the last year in our study population. It was noted that the rate of none/incomplete vaccination was higher in those hospitalized patients for pneumonia. Also, it was found that not only the pneumococcal vaccine but also BCG, OPV, and MMR vaccines were implemented at a lower rate in this group. Another remarkable result was that influenza vaccination was recommended for patients hospitalized due to pneumonia at a higher rate, and patients were administered influenza vaccine more common. This may be because preventive implementation and vaccines are considered more frequently during follow-up in patients hospitalized due to pneumonia.

Advisory Committee on Immunization Practices recommended influenza vaccine for people with chronic pulmonary, cardiovascular, renal, hepatic, neurological, hematological, metabolic diseases or immunocompromised people in their recommendations for 2020–2021 Control of Seasonal Influenza with Vaccines (13). In a cohort study by Keren et al., 322 of 745 patients with laboratory-confirmed influenza, had one or more chronic diseases. Neurological and neuromuscular diseases are independent risk factors for respiratory failure (14). In another study of 830 pediatric deaths associated with laboratory-confirmed influenza reported to the Center of Disease Control between October 2004 and September 2012, an underlying neurological disease was found at a rate of 33% (15). In the meta-analysis by Gill et al. in 2014, in 27 studies involving 14086 patients, neurological diseases were accepted as a high-risk factor for influenza-related hospitalizations (16). In a study by Pandolfi et al., among 275 patients with chronic diseases, the lowest vaccination rate for influenza vaccine was found in patients with a neurological disease with 25% (17). Considering that the frequency of influenza vaccination is generally low in our country, it is low in patients with CP, who are in the risk group. In our study, only 3.4% of the patients with CP were vaccinated against influenza throughout their lives. Similarly, only 2.6% of the patients were vaccinated during the season of the study. In a study from our country, Dinleyici et al. evaluated the vaccination of 366 patients with chronic neurological disease and found that 86.6% of patients had never been vaccinated against influenza in their life (5). Although it is not as rare as in our country, there are examples of missing vaccination opportunities for these patients in other countries in the literature. In a study from the US, Havers et al. evaluated the vaccination records of 184460 patients with ≥ 1 neurological disease(s) between 2006 and 2014. They found that even in the 2013–2014 season when vaccination was the highest, less than half of the patients and 1/3 of these in the 10–17 years age group were vaccinated against influenza (18). Worldwide, we need to develop interventions to

increase the vaccination rates of the patients with CP who are in the risk group for influenza complications.

CP develops in the fetal or infant brain causing activity restriction and is not progressive. It is a group of diseases that affects movement and posture (19). In a study conducted by Serdaroğlu et al. with 41861 children aged between 2–16 years in our country, the prevalence of CP was reported as 4.4 per 1000 live births (20). Patients may encounter many problems commonly seen in this disease, e.g., intellectual disability, behavioral disorders, epilepsy, somatosensation disability, visual and auditory disorders, orthopedic deformities, gastrointestinal and nutritional problems. The most common concomitant diseases were epilepsy, orthopedic problems, and growth retardation in our study population. More than half of patients who present to our study have severe motor dysfunction, which makes it difficult to move. Children with CP who had higher levels of motor dysfunction (level 4 and 5) were more likely to be overdue immunizations. A study from Canada (9) showed that children with moderate to severe disabilities are less likely than those with a mild disability to have received a basic series of immunizations. Similarities in this study and those observed associations between severe motor dysfunction and vaccination prompted us to investigate the potential role of the immunization status of this disease. In our study, the vaccination rate of hepatitis B, BCG, DTaP-IPV-Hib, OPV, and MMR was statistically significantly lower in patients with severe motor dysfunction. The clinical picture of the association between low vaccination rate and severe motor dysfunction is most likely a result of a complex interplay between direct and indirect effects of CP. It may be that this group of children have an ongoing severe chronic illness resulting in frequent hospitalizations delaying age-appropriate immunizations or that the high level of care required may limit the time available for immunization appointments. Or, vaccines may have been neglected because the physicians who follow patients are concerned with other medical problems. Despite our results, Greenwood et al. demonstrated no association with motor dysfunction level and vaccination rate (10). They discussed that the results may have been influenced by survival bias as most children who died were severe motor dysfunction, and the immunization records for these children had been removed from their national database.

Barriers to vaccination of patients with CP are familial factors and false contraindications of both parents and healthcare professionals. The most important reason for incomplete vaccination in our study was due to primary school vaccination in children. Therefore, we think that the administration of primary school vaccinations from primary care physicians and the development of a catch-up vaccination schedule for those patients without an age-appropriate vaccination will be of great benefit in protecting against diseases and increasing the quality of life in children with CP. One study concluded that some parents may be concerned that the possible adverse outcomes of immunizations may outweigh the potential benefits, such as increasing frequency of seizures and a small proportion of parents may believe that immunizations contributed or caused their child’s disability (10). These concerns were rarely mentioned by the parents of our patients.

Conclusion

Although the management of CP is not curative, it is a disease in which the quality of life of patients and their relatives can be increased with an appropriate approach. One of the most important approaches to achieve increasing the quality of life is the prevention and control of infections, including vaccination. This study demonstrates that children with CP have a high risk of incomplete and delayed immunization, a significant concern given to their increased healthcare needs and vulnerability to infectious diseases. Consequently, providing information to parents and clinicians following these patients on influenza and other vaccination practices are important, not only for the vaccination of these children but also of their parents. And also, the clinician must be aware of immunization status both in outpatients and inpatients of children with CP. Investigations can include immunization cards, and awareness to none/incomplete vaccination both including and excluding NIP. Only in this way will it be possible to increase the rates of vaccination in the CP population.

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Tables

Table 1. Etiology and characteristics of cerebral palsy

Etiology*	n	%
Asphyxia	474	39.7
Prematurity	473	39.6
Structural abnormalities	81	6.8
Intracranial hemorrhage	76	6.4
Metabolic encephalopathy	58	4.9
Multiple births	53	4.4
Meningitis encephalitis sequela	38	3.2
Head injury	22	1.8
Intrauterine infections	13	1.1
Others	18	1.5
Unknown origin	96	8.0
Clinical category		
Spastic	996	83.4
Atonic	54	4.5
Dyskinetic	40	3.4
Mixed	56	4.7
Missing data	48	4.0
Topography		
Quadriplegic	349	29.2
Hemiplegic	206	17.3
Paraplegic	138	11.6
Diplegic	84	7.0
Monoplegic	6	0.5
Missing data	411	35
Gross motor dysfunction		
Level 5	503	42.1
Level 4	140	11.7
Level 3	184	15.4
Level 2	181	15.2
Level 1	115	9.6
Missing data	71	5.9

*Some patients may have more than one cause

Table 2. Demographical and clinical characteristics of patients with CP

Characteristics	
Age[a]	93.9 ± 57.6
Gender (male)[b]	689 (57.7)
Concomitant diseases[b]	959 (80.3)
epilepsy	671 (56.2)
orthopedic problems	500 (41.9)
growth retardation	348 (29.1)
visual disorders	182 (15.2)
recurrent pneumonia	116 (9.7)
auditory disorders	33 (2.8)
Using medications[b]	763 (63.9)
antiepileptics	528 (44.2)
antiepileptics + muscle relaxants	105 (8.8)
muscle relaxants	81 (6.8)
antipsychotics	13 (1.1)
antiepileptics + antipsychotics	11 (0.9)
muscle relaxants + antipsychotics	4 (0.3)
antiepileptics + muscle relaxants + antipsychotics	2 (0.2)
others	19 (1.6)
Hospitalization in the last year[b]	342 (28.6)
Hospitalization in the last year due to pneumonia[b]	178 (14.9)

[a] Values were given as mean ± SD, [b]Values were give as percentage

Table 3. Age-appropriate vaccination according to the National Immunization programme

Vaccines	Completed	Incomplete	None
Hepatitis B	1062 (88.9)	41 (3.4)	91 (7.6)
BCG[a]	1084 (90.8)	-	110 89.2)
DTaP-IPV-Hib[b]	722 (60.5)	379 (31.7)	93 (7.8)
OPV[c]	1057 (88.5)	26 (2.2)	111 (9.3)
Pneumococcus	646 (54.1)	181 (15.2)	367 (30.8)
MMR[d]	923 (77.3)	111 (9.3)	160 (13.4)
Varicella	583 (48.8)	-	611 (51.1)
Hepatitis A	492 (41.2)	52 (4.4)	650 (54.4)

[a]Bacillus Calmette-Guerin, [b]Diphtheria, Tetanus, acellular Pertussis - Inactivated Polio vaccine - Haemophilus influenzae type B, [c]oral polio vaccine, [d]measles-mumps-rubella

Figures

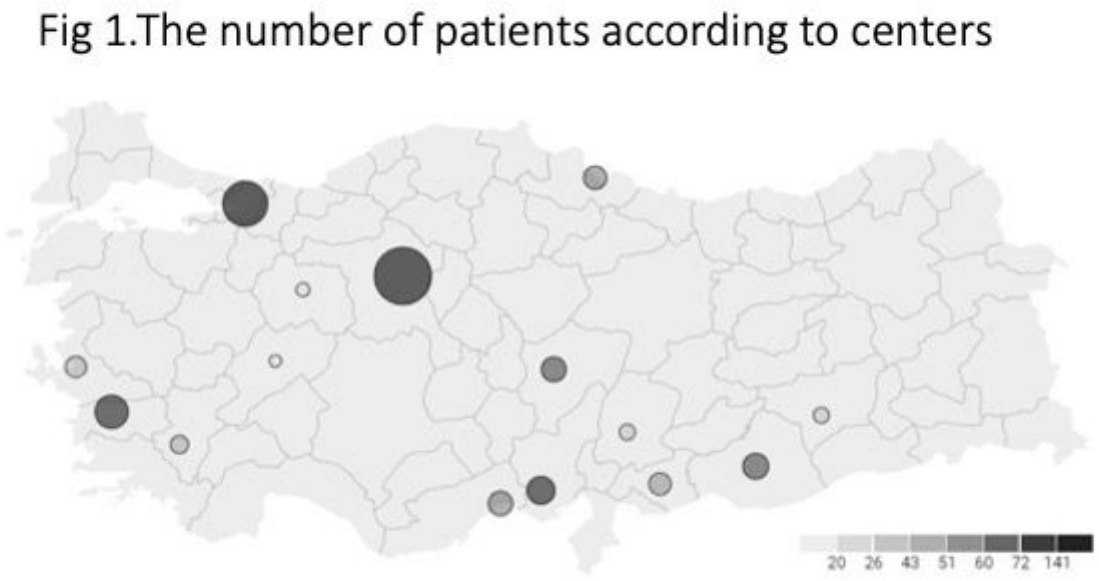

Figure 1

The number of patients according to centers was shown in Figure 1.