

An epidemic caused by measles virus type D6 in Turkey

Ali Ceylan¹, Melikşah Ertem¹, Gülay Korukluoğlu², Hamit Acemoğlu¹

İsmail Hamdi Kara³, Pakize Gamze Erten³, Cem Arslan⁴, Mehmet Emin Ay⁵

Departments of ¹Public Health and ³Family Health, Dicle University Faculty of Medicine, Diyarbakir; ²Refik Saydam Central Hygiene Institute, Ankara; ⁴Cizre Health Center, Cizre Sırnak; and ⁵Idil Health Group, Idil Sırnak, Turkey

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In this study, the extent of measles outbreak was investigated in the Idil and Cizre counties of Sırnak Province. New cases determined in patients who applied to primary care clinics and those detected during home visits were evaluated. In 2001, a total of 2,143 cases reported in Sırnak Province were signified as a probable outbreak. Three hundred and thirty-three patients in Cizre and 219 patients in Idil applied to the primary care clinics. Of the cases, in Cizre 8.4% (n=28) and in Idil 6.4% (n=14) were infants aged nine months and younger who had not yet been vaccinated. Totally, 17 new cases (8 in Cizre and 9 in Idil) in the exanthema phase were determined during home visits and these were considered as outbreak cases. Virus isolation was achieved in 12 cases. All isolates were sent to the Centers for Disease Control (CDC) for genotyping and classified as D6 group. In conclusion, measles epidemics are still seen in our country. Therefore, measles outbreaks necessitate intensive intervention by physicians who are employed in primary health care services.

Key words: measles, outbreak, immunization, infant, developing country.

Measles remains a leading cause of childhood mortality worldwide, accounting for 5% of all deaths among children aged less than five years. Measles thus accounts for nearly one-half of the 1.7 million annual deaths due to childhood vaccine-preventable diseases¹.

Measles virus is present during the acute stage in throat and nasopharyngeal secretions for up to four days and is excreted in urine for at least seven days after rash onset. Virus isolation should be attempted for all sporadic cases of measles and for cases occurring early in a measles outbreak².

In developing countries with a high level of infection, infants below the age of 12 months are at high risk for measles virus (MV) infection. In this age group passively transferred maternal immunoglobulins (Ig) pose a problem because declining maternal antibodies interfere with vaccine-induced seroconversion but do not protect against infection with wild-type MV³⁻⁶.

Worldwide, measles vaccination has been very effective, preventing an estimated 80 million cases and 4.5 million deaths annually. The World Health Assembly in 1989 and the World Summit for Children in 1990 set goals for measles morbidity and mortality reduction of 90% and 95%, respectively, compared with prevaccine levels⁷. Subsequently, target dates for measles elimination in three WHO regions, the Americas and the Eastern Mediterranean, were set for 2000, 2007 and 2010, respectively⁸.

In Turkey, children are vaccinated against measles at nine months of age routinely. Goal number 25 of the National Health Politics Document published by the Ministry of Health in March 1993 was nationwide eradication of measles by 2005⁹.

In the present study, it was aimed to investigate measles outbreak in Cizre and Idil counties of Sırnak Province in Turkey between January and July 2001 and to identify the applications carried out by primary care physicians for controlling outbreak.

Material and Methods

In the present study, the extent of measles outbreak was investigated in two counties of southeast Turkey in 2001. The Southeastern Anatolia region covers 9.7% of the lands in Turkey, with a surface area of 75,000 km². Medical facilities are concentrated in the cities and larger towns, leaving most rural areas without adequate access to medical care¹⁰. There are six district and two primary care clinics in Cizre, which has a population of 100,000. Idil's population is approximately 13,000 and it has one primary care clinic. In 2001, the estimated population of Sırnak Province was 353,000.

In this article, the term 'outbreak' is used to ensure consistency when referring to any increase in the occurrence of measles cases in a community above the number expected. The academic personnel of Dicle University Faculty of Medicine Public Health Department conducted home studies in conjunction with the Southeast Anatolia Public Health Project Field Study, during which households were asked "Who recently became ill in your home?". The probability of a measles outbreak in Cizre and Idil counties was suspected because of the great number of responses regarding acquisition of measles by children. A study was then planned to investigate measles in centers of Cizre and Idil counties of Sırnak Province. This measles outbreak in 2001 primarily affected an important part of Southeast Anatolia.

Firstly, in order to understand whether there was an outbreak, the polyclinic records of primary care clinics were investigated together with the physicians of Cizre primary care clinics (numbered as 1 and 2) and of the one Idil center primary care clinic, and the number of measles cases among patients who applied to primary care clinics between January-July 2001 was determined. Later, measles and outbreak subjects were discussed in a meeting held with the personnel of each primary care clinic, where information about the outbreak investigation was provided.

Crews formed by physician, nurse and/or midwife were constituted, and home visits were conducted. Crews formed of two personnel visited homes to search new patients, determine those who could be protected or treated, and to establish the true extent of the outbreak.

Laboratory Methods for Diagnosing Measles and Virus Isolation

Patients accepted as cases of measles included those with fever, coryza, conjunctivitis, Koplik's spot and maculopapular erythematous rash at first on the face, which later became generalized. Clinical specimens as throat swab, urine and blood were collected from suspected cases at the beginning period of rash for serodiagnosis and isolation of MV and were kept at +4°C. All samples were sent to the National Measles Laboratory, Refik Saydam National Hygiene Center in 24 hours. In the laboratory, sera samples were tested with a commercial capture IgM ELISA kit (Enzygnost, Dade-Behring, Germany) and clinical samples were inoculated into COBL cell line for isolation. Twelve of 26 patients were thus confirmed as measles cases. On the other hand, all isolates were identified as MV with neutralization method using measles specific anti-H monoclonal antisera and COBL cell line. All isolates were sent to Centers for Disease Control (CDC) for genotyping and classified as D6 group.

Results

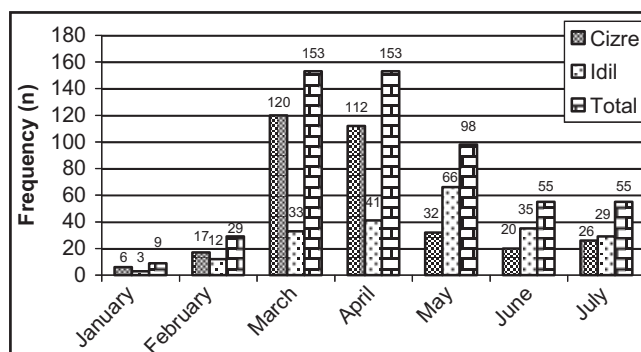
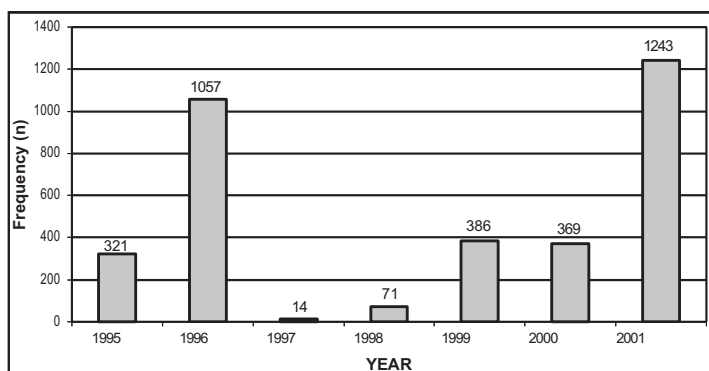
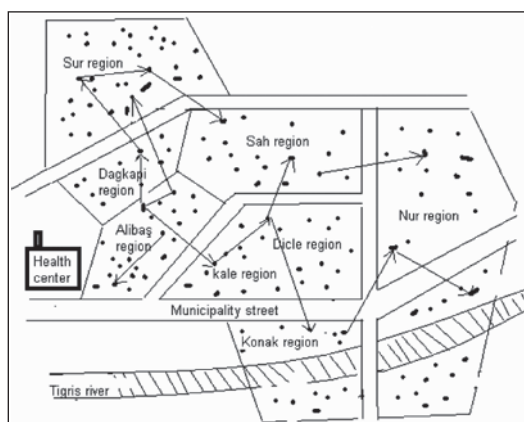
In the present study, an outbreak investigation was carried out in the centers of Cizre and Idil counties. Table I shows age and gender distributions of the patients who applied to primary care clinics in Idil and Cizre between January and July 2001.

The distribution of the patients who applied to the primary care clinics for measles according to months is seen in Figure 1. While six cases were seen in Cizre in January, the number of the patients peaked in March, reaching 120. In Idil, the peak was seen in May with 66 cases (30.1%). Moreover, 31 patients applied to primary care clinics from villages of Idil, and 80.6% of the applications (n=259) were in May, June and July.

Figure 2 shows measles cases reported to Sırnak Province Health Directorate between 1995 and 2001. According to this data, the 1,050 cases reported in 1996 indicated an outbreak. In Cizre, the first case applied to primary care clinic 2 on 3 January 2001 from the Alibas district, and the disease then spread to the Kale and Sur districts, and by March the applications had become widespread (Fig. 3).

Table I. Age and Gender Distribution of the Patients Who Applied to Primary Care Clinics for Measles in Idil and Cizre (January-July 2001)

Age group	Cizre		Idil		Total	
	n	%	n	%	n	%
0-9 mos	28	8.4	14	6.4	42	7.6
10 mos-4 yrs	250	75.1	156	71.2	406	73.6
5-9 yrs	50	15.0	40	18.3	90	16.3
10+	5	1.5	9	4.1	14	2.5
Gender						
Male	186	55.9	128	58.4	314	56.9
Female	147	44.1	91	41.6	238	43.1
Total	333	100	219	100	552	100.0

**Fig. 1.** Distribution of measles cases by month in Cizre and Idil counties of Şırnak Province.**Fig. 2.** Distribution of cases of measles by year in Şırnak Province.**Fig. 3.** Spot map of measles outbreak in Cizre county.

The first application in Idil was from the Atakent district, and the disease later spread to the Yeni district and then to the whole county (Fig. 4).

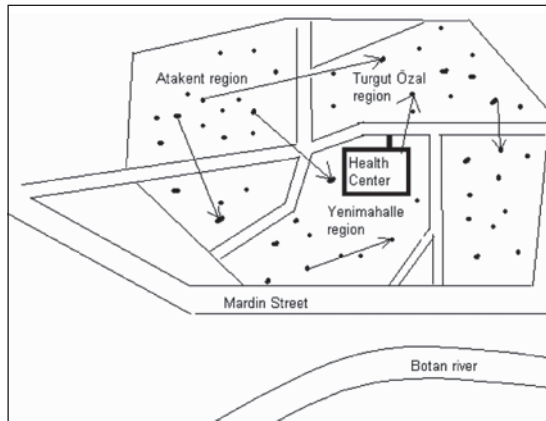


Fig. 4. Spot map of measles outbreak in Idil county.

(Table II). On the other hand, all isolates were identified as MV with neutralization method using measles specific anti-H monoclonal antisera and COBL cell line. All isolates were sent to CDC for genotyping¹¹.

The new cases were examined thoroughly, and antibiotics, analgesics and antiallergic drugs were given if necessary. The 123 children who had not yet contracted measles and were living in households where no one was previously affected by measles were vaccinated once. An outbreak report was prepared together with the physicians of the primary care clinics that included the cases recorded in the primary care clinics but not reported together with the newly diagnosed cases.

At home visits, the children who contracted measles during 2001 were evaluated about application to primary care clinics, measles vaccination conditions, and factors contributing

Table II. Symptoms, Vaccination and Virus Isolation Status of the Confirmed Cases

Case No.	Age (yrs)	Vaccination	Symptoms			Specimens			Serology	
			Fever °C	Rash	Koplik Spot	Throat Swab	Urine	Blood	Ig M	Ig G
1	4.5	Yes (1 dose)	+	+	-	+	-	+	+	-
2	3	No	+	+	-	+	+	+	-	-
3	1	No	+	+	-	+	-	+	+	-
4	3	No	+	+	-	+	-	-	+	-
5	2	No	+	+	-	+	-	-	+	-
6	3	Yes (1 dose)	+	+	-	+	+	+	+	-
7	4	Yes (1 dose)	+	+	-	+	-	+	+	-
8	2	No	+	+	-	-	+	-	+	-
9	8 mos	No	+	+	-	+	-	+	+	-
10	7	No	+	+	-	+	+	+	+	-
11	2.5	No	+	+	-	+	-	+	+	-
12	7	No	+	+	-	+	+	+	+	-

In Cizre, the average numbers of household members and of children under the age of 10 years were found to be 11.3 ± 5.8 and 4.2 ± 2.2 , respectively, while for Idil the numbers were 9.8 ± 4.8 and 3.9 ± 2.1 , respectively. Children under the age of 10 years constituted 38.4% of the whole population.

Totally 17 new cases (8 in Cizre and 9 in Idil) in the exanthema phase were determined during home visits, and these were considered as outbreak cases. Throat swabs, urine and blood specimens were taken from these cases in order to perform virus isolation and confirmation and were sent to Refik Saydam National Hygiene Center-Measles Laboratory, Ankara, Turkey. Virus isolation was achieved in 12 cases

to disease acquisition. According to this data, almost all sufferers consulted physicians and none of the cases resulted in death. When features of the children were investigated, it was found that age, vaccination status and the district of residence were contributory factors in acquiring measles. Furthermore, of those children previously vaccinated, 59 (35.8%) in Cizre and 13 (10.2%) in Idil were affected by the outbreak.

Discussion

The measles outbreak in rural Siirnak Province began in January 2001 in two settlements in close proximity; therefore, there was frequent and regular movement and contact between

the two settlement populations. Of the 552 patients who applied to the primary care clinics, 333 were from Cizre and 219 were from Idil, and the ratios of the children aged less than or equal to nine months who were too young for vaccination were 8.4% ($n=28$) and 6.4% ($n=14$), respectively. On the other hand, 74.9% ($n=250$) of cases in Cizre and 71.2% ($n=156$) of cases in Idil were aged between 10 months and four years, and 56.9% ($n=314$) were male and 43.1% ($n=238$) female (Table I).

In Cizre, the index case applied to primary care clinic 2 on 3 January 2001 (Fig. 3), while in Idil the first application was seen on 23 January (Fig. 4). The peak application levels were observed in March and April in Cizre and in May in Idil (Fig. 1).

The course of the outbreak might have been affected by personnel (place of occupation changed frequently or because of the excessive number of temporary health personnel). It is important that according to primary care clinic records, 7.4% of the affected patients ($n=39$) were children 0 to 9 months of age who were unvaccinated. This ratio is in accordance with the findings of Ertem et al.¹², who determined that 6.7% of the cases were below nine months when the measles outbreak occurred in the center of Diyarbakir, Southeast Turkey, in 1996.

From 2001 to the present, there has been no significant increase in the number of measles cases, and there was no new outbreak in the region. This may be attributable to the increase in vaccination coverage in the region, which was improved via education of health staff.

The World Health Organization recommends that vaccination against measles normally be undertaken at the age of nine months; however, it was considered that measles epidemics have occurred every two to five years in developing countries such as Turkey (Fig. 2). In this respect, during a measles epidemic, if a large proportion of cases occur in children below nine months (i.e., the attack rate for children <9 months is high), the age of measles immunization should be temporarily lowered to six months. Because of the lower efficacy of the vaccine at this age, these children must be re-immunized as soon as possible after nine months¹³⁻¹⁵.

During home visits to determine new and contact cases during the outbreak, it was determined that at least one child had

contracted measles in 60% and 38% of the homes in Cizre and Idil, respectively. This may have been due to the high number of household members, and consequently to a high number of non-immunized children. Furthermore, according to the mothers, the ratio of vaccinated children is low in Cizre; of the children below 10 years, 55.3% in Cizre and 26.5% in Idil were non-immunized.

During their research of the measles outbreak in 1993, which occurred in the region of Güzelbahçe primary care clinic of Izmir Province, Turkey, Ellidokuz et al.¹⁶ determined that 68.6% of the measles cases aged 0 to 14 years had been vaccinated before. Ertem et al.¹² found that 26.7% of the measles cases in Diyarbakir were vaccinated children. Mutlu et al.¹⁷ searched the vaccination status of measles cases in Izmir and revealed their vaccination ratios by year. According to this data, in 1988, 49%, in 1989, 42%, in 1990, 41%, in 1991, 49%, in 1992, 48%, and in 1993, 57% of the cases had been vaccinated before. In our study, the vaccination status of the cases was 42.1% in Cizre and 13.5% in Idil. The statistic is meaningful because it raises the question of the insufficiency of the vaccine and the necessity of readdressing the measles vaccination schedule.

The measles-containing vaccines currently in use are safe and effective, though not 100% effective. In countries where immunization is undertaken at 12-15 months of age, measles vaccine efficacy is estimated to be between 90% and 95%. In countries where the first dose is given at nine months, vaccine efficacy is estimated to be approximately 85%. Despite the widespread availability of a safe and effective vaccine for over 30 years, failure to administer at least one dose of measles vaccine to all infants continues to be the main cause of measles mortality and morbidity. A high proportion of vaccine preventable cases in an outbreak would suggest that failure to vaccinate children was a significant factor. Spot maps, demographic information and age-specific attack rates can help to identify reasons for a failure to vaccinate¹³⁻¹⁵.

A study of Aylward et al.¹⁸ illustrates the limited amount of data that has been published on measles outbreak immunization activities in middle and low-income countries. The

data that are available, however, suggest that outbreak immunization activities in developing countries do not have a significant impact on the course of measles epidemics. Because infants in developing countries may receive measles vaccine under suboptimal conditions, the efficacy can be significantly lower than that observed in industrialized countries.

In 2001, the number of confirmed measles cases in the region of the Americas reached a record low of 537 cases, a 99% decrease since 1990^{19,20}. In 2001, the Dominican Republic and Haiti interrupted indigenous measles transmission successfully^{20,21}, ending known indigenous transmission of the D6 MV genotype. This genotype, which had circulated widely in the region of the Americas since 1995, caused nationwide outbreaks in Argentina, Bolivia, Brazil, the Dominican Republic, and Haiti during 1997-2001²⁰⁻²³. In August 2001, a measles outbreak introduced by a traveler returning from Europe occurred in Venezuela and was exported to Colombia in 2002¹⁹. In our study, a total of 17 new cases (8 in Cizre and 9 in Idil) were determined during home visits, and these were considered as outbreak cases. Measles IgM antibodies were found to be positive in 11 of 12 virus isolated patients (Table II). All isolates were sent to CDC for genotyping and also classified as D6 group¹¹.

During 1989 and 1990, reported measles cases in the United States increased 6- to 9-fold over the annual mean of 3,000 between 1985 and 1988. There were 815 outbreaks, accounting for 94% of the 52,846 cases reported. Similar to that observed in 1985 and 1986, three patterns of measles transmission during outbreaks were identified: (1) predominantly among unvaccinated pre-school aged children <5 years of age (38% of outbreaks); (2) predominantly among vaccinated school aged children 5 to 17 years of age (40%); and (3) predominantly among unvaccinated and vaccinated post-school aged persons <18 years of age (22%). Recent epidemiology suggests that to achieve elimination of measles, ACIP recommendations must be fully implemented, including (1) routine administration of the first dose of measles vaccine from 12 to 15 months of age and (2) use of a routine two-dose schedule to prevent school age and post-school age outbreaks²⁴.

Dicle University was involved in the survey of the measles cases. A new strategy, which is based on active surveillance of the cases, was conducted with the contribution of the Health Director of Sirnak Province. Also, a modular education program on vaccination developed by the Ministry of Health was applied to the primary health care staff of Sirnak Province. Dicle University participates in these education sessions. A new project regarding surveillance of measles is also planned in the region.

In conclusion, measles epidemics are still seen in our country. Therefore, measles outbreaks necessitate intensive intervention by physicians who are employed in primary health care services. Measures to control measles outbreaks in Southeast Turkey must include 1) partnerships with local municipalities, 2) rapid identification and vaccination of groups at high risk, 3) an additional dose at 6-9 months for infants at high risk, 4) house-to-house monitoring of vaccination coverage, and 5) heightened surveillance in all regions of the country.

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