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ANALYSIS OF MEASLES CASES IN A UNIVERSITY PEDIATRIC HOSPITAL DURING 1988 AND 1993 OUTBREAKS*

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SUMMARY: Oğuz F, Sıdal M, Uzel N, Özgeneci A. (Department of Pediatrics, İstanbul University Faculty of Medicine, Çapa-İstanbul, Turkey). Analysis of measles cases in a University Pediatric Hospital during 1988 and 1993 outbreaks. Turk J Pediatr 1995; 37: 83-92.

In Turkey, a mass measles immunization campaign was initiated in 1985, and the decision was made to administer the first of the measles vaccinations at nine months of age instead of 12-15 months. Following the campaign there was a decrease in the number of measles cases seen in the Outpatient Department of İstanbul University Children's Hospital in 1986 and 1987; however, after 1987 an increase was observed in measles cases, which continued until 1993.

In order to investigate the current measles epidemics, we reevaluated the measles cases seen in our Outpatient Department from 1986 to 1993. We also investigated the vaccination status and the hospitalization and mortality rates of measles cases in the epidemics of 1988 and 1993.

Since 1988 (except 1989) a significant increase (412-1375 percent) has been observed in measles cases, and between 1986 and 1993 more than half of all measles cases were in children older than four years of age. In 1988 and 1993 we found that most vaccinated measles cases were also in this age group, but the rate of complications and hospitalization among the vaccinated cases was lower compared to those who were not vaccinated. *Key words: measles, vaccinated measles cases, measles complication, measles mortality.*

Despite the fact that measles vaccination has become a standard public health procedure since 1963, the disease continues to be a major cause of morbidity and mortality[1-4]. WHO recommends that underdeveloped and developing countries start administering the measles vaccination at nine months of age[5, 6].

In Turkey, a mass measles immunization campaign was initiated in 1985, and the decision was made to administer the first measles vaccination in the series at nine months of age instead of 12-15 months.

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In 1983, before the campaign, measles vaccination rates were 12.3 percent for nine-to-12-month-old children, and 36.5 percent for children ≤ 5 years old. With the campaign this rate had been increased to 72.4 and 82.5 percent respectively[7].

After that campaign the number of measles cases seen in the Outpatient Department of Çapa Children's Hospital, University of İstanbul, declined in 1986 and 1987[8]. But there was an increase in 1988 which continued until 1993 (except in 1989 when no increase was noted).

In order to determine the characteristics of the measles cases that have been seen in the Outpatient Department from 1986 to 1993, their records were reevaluated.

Material and Methods

At the Outpatient Department of Çapa Children's Hospital, University of İstanbul, patients aged 0 to 16 years receive an examination card and acquire a file in the computer. Diseases that should be declared are reported to the National Notifiable Disease Surveillance System.

The number of measles cases diagnosed in the outpatient clinic from 1986 to 1993 was determined from the annual outpatient data and statistics. The characteristics of the measles cases that had been seen in 1988 and 1993 in the outpatient department were determined by a retrospective review of the records of measles patients. The diagnosis of measles was made when there was a generalized maculopapular rash lasting three days or more, fever of 38.3 °C or greater, and the presence of a cough, coryza or conjunctivitis[9]. The records of hospitalized measles cases in 1988 and 1993 were also reviewed retrospectively.

Frequency of disease, complications, hospitalization, mortality rates, vaccination situation and clinical data were assessed in two age groups, namely ≤ 4 years and ≥ 5 years of age. Monthly distribution of disease was also investigated. Chi-square test was used in the statistical analysis.

Results

Although the number of measles cases seen in the Outpatient Department decreased in 1986 and 1987 (0.08% of all clinical cases), a peak was observed in 1988 (0.75%). The significant decrease in number (0.08%) in 1989 was followed by a slight increase (0.41%) in 1990 and another peak (1.18%) in 1991. This increase continued slowly in 1992 (0.87%) and reached a rate in 1993 similar to that of 1991 (1.13%). Although the aim of the study was not epidemiological, our hospital findings are in concordance with the data of İstanbul Province Health Directorate (unpublished information), only on a smaller scale (Fig. 1).

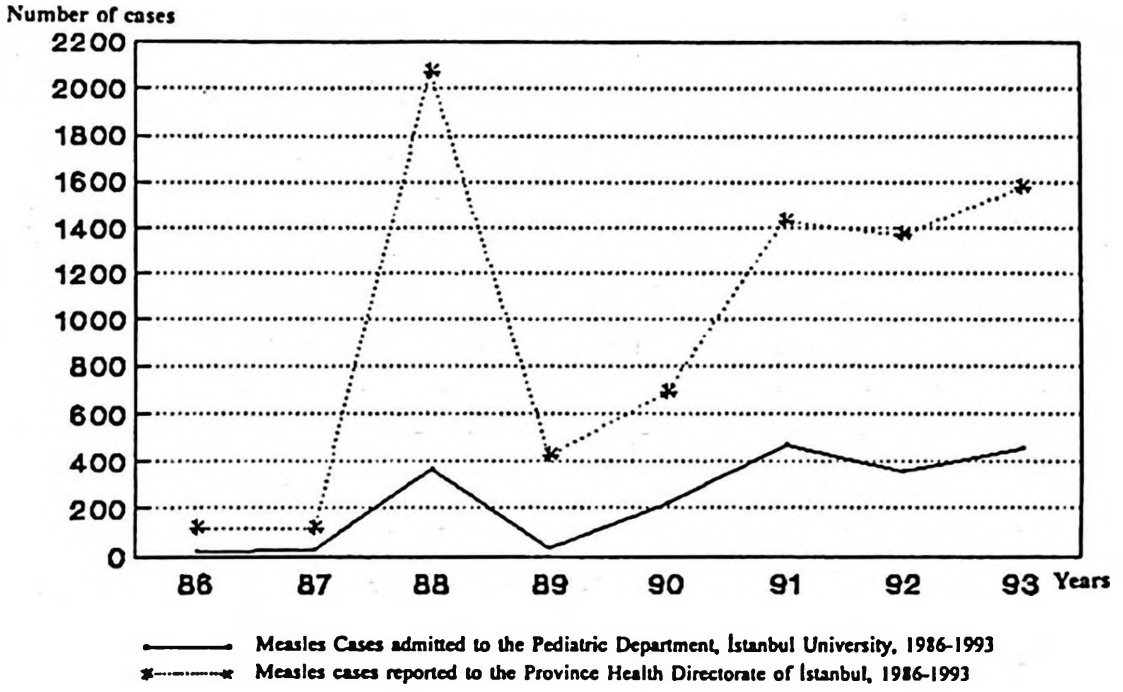

Fig. 1: The distribution of measles cases at outpatient clinics and at the Province Health Directorate of İstanbul.

Between 1986 and 1993, more than half of all measles cases were in children older than four years of age (Table I).

Table I: Age Distribution of Measles Cases, 1986 to 1993

	Number of Measles Cases		
Years	≤ 4 Years n (%)	≥ 5 Years n (%)	Total n
1986	8 (42.1)	11 (57.9)	19
1987	10 (41.7)	14 (58.3)	24
1988	154 (42.0)	213 (58.0)	367
1989	14 (40.0)	21 (60.0)	35
1990	96 (43.8)	123 (56.2)	219
1991	213 (45.9)	251 (54.1)	464
1992	151 (42.3)	206 (57.7)	357
1993	200 (44.1)	254 (55.9)	454

The decrease in measles epidemics observed in 1986 and 1987 was followed by an increase in 1988. Of the cases observed during the epidemics in 1988 and 1993, 42 percent of the cases in 1988 and 44 percent of the cases in 1993 were among younger children (≤ 4 yrs). Children in the 0-12-months-old group that were younger than nine months and consequently had not yet been vaccinated comprised 4.1 and 5.1 percent of the cases, respectively, in 1988 and 1993 (Table II). Two hundred sixtyfour (72%) of 367 measles cases in 1988, and 257 (56.6%) of 454 measles cases in 1993 had documentation of vaccination

against measles. In 1988, 44.7 percent of the 264 cases had a known history of vaccination and 57.3 percent of the 257 cases constituted vaccinated children in 1993. When these rates were compared, although high in both periods, the rates were found to be significantly higher in 1993 than in 1988 ($x^2 = 5.918224$, $p < 0.05$). The increase in 1993 was statistically significant only for the age group of ≤ 4 years ($x^2 = 5.189795$ $p < 0.05$) (Fig. 2).

Tablo II: Age Distribution of Measles Cases, 1988 and 1993

	Number of Measles Cases			
	1988		1993	
Age	n (%)		n (%)	
0-12 months	55[1] (15.0)		76[2] (16.7)	
		(42.0)		(44.0)
13 months-4 years	99 (27.0)		124 (27.3)	
≥ 5 years	213 (58.0)		254 (56.0)	
Total	367 (100.0)		454 (100.0)	

1.15 cases < 9 months.
2.23 cases < 9 months.

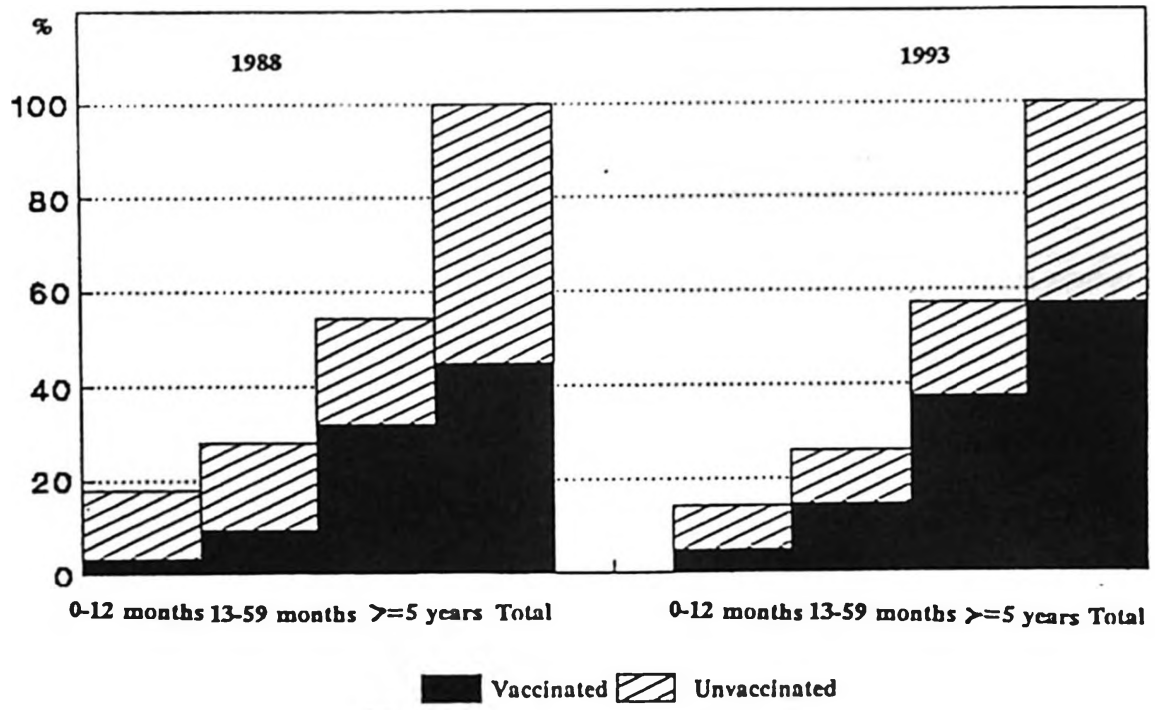

Fig. 2: Rates of vaccinated measles cases

The rate of the vaccinated measles cases correlated positively with the age of the children, and it was significantly higher in the ≥ 5 year-old children in 1988 ($x^2 = 23.67166$ $p < 0.001$) and 1993 ($x^2 = 16.12432$ $p < 0.001$). On the other hand, of measles cases with a known history of vaccination, 46.9 percent in 1988 and 45 percent in 1993 were children < 5 years of age (Fig. 2). Of unvaccinated

measles cases < 5 years old, 59.5 percent in 1988 and 37.5% in 1993 were of vaccine-eligible age (> 9 months).

Complications were noted in 36 percent of the cases in 1988 and 44.9 percent of the cases in 1993. The elevation in 1993 was found to be statistically significant ($x^2 = 638325$ $p < 0.05$). Among the vaccinated cases, a slight increase in the number of complications was observed in 1993 compared to 1988, but the difference is not statistically significant ($x^2 = 2.2233695$, $p = 0.1$).

As for the distribution of the complicated cases according to age, the rates were found to be higher in children ≤ 4 years of age in both 1988 and 1993. The complication rate was significantly higher in unvaccinated children compared to vaccinated children in 1988 ($x^2 = 38.18582$ $p < 0.001$) and 1993 ($x^2 = 29.52505$ $p < 0.001$) (Table III). In both years, the complication noted in over two-thirds of the cases was bronchopneumonia.

Table III: Age-Specific Measles Complication Rates in Vaccinated and Unvaccinated Children, 1988 and 1993

	Complication Rates					
	1988			1993		
Age	Vaccinated n (%)	Unvaccinated n (%)	Total n (%)	Vaccinated n (%)	Unvaccinated n (%)	Total n (%)
0-12 monts	1 (11.1) (29.4)[1]	27 (71.0) (65.5)	29 (52.7) (51.9) [60.2][2]	3 (23.1) (42.0)[1]	29 (80.6) (77.3)	48 (63.2) (64.0) [62.7][2]
13 months - 4 years	9 (36.0)	30 (61.2)	51 (51.5)	18 (48.7)	22 (73.3)	80 (64.5)
≥ 5 years	12 (14.3)	26 (44.1)	52 (24.4) [39.4]	19 (19.6)	17 (38.6)	76 (29.9) [37.3]
Total	22 (18.6)	83 (56.8)	132 (36.0)	40 (27.2)	68 (61.8)	204 (44.9)

1. Measles complication rate in 0-4 years age-group.
2. Percentage of complication in certain age-groups among total complications.

The percentage of patients hospitalized and treated due to severe complications was similar in 1988 and 1993 (4.4%) (Table IV). In 62.5 percent of cases in 1988 and 80 percent of cases in 1993, the reason for hospitalization was bronchopneumonia; the rest had been hospitalized for encephalitis. Encephalitis was observed mainly in ≥ 5-year-old children. Of hospitalized cases in 1988 and 1993, 68.8 and 70 percent, respectively, were children ≤ 4 years old. None of the cases died in 1988, and only one patient died due to bronchopneumonia in 1993. The rate of hospitalization for vaccinated children was equal in both years and significantly lower than for those not vaccinated. (For 1988, $x^2 = 4.308483$ $p < 0.05$ and for 1993, $x^2 = 8.196599$ $p < 0.01$).

In conclusion, although the number of vaccinated measles patients and the rate of complications was higher in 1993, the distribution of the cases by age-group

and complication rate as well as the findings of the hospitalized cases were similar in both years. As expected, the rate of hospitalization and complications among the vaccinated cases was lower than in those not vaccinated. Another point in common was the monthly distribution of the cases. In both years, measles cases occurred with a very low incidence in January. A small increase in February and March and a peak in May were observed (Fig. 3). Cases diagnosed between April and June comprised 88.4 percent of all measles cases in 1988 and 67.9 percent of all measles cases in 1993.

Table IV: Age-Specific Measles Hospitalization Rates in Vaccinated and Unvaccinated Children, 1988 and 1993

	Hospitalization Rates					
	1988			1993		
Age	Vaccinated n (%)	Unvaccinated n (%)	Total n (%)	Vaccinated n (%)	Unvaccinated n (%)	Total n (%)
0-12 monts	0 (0)	3 (7.9)	3 (5.5) (18.8)[2]	0 (0)	6 (16.7)	6[1] (7.9) 30.0
	(2.9)	(9.2)	(7.8) (68.8)	(4.0)	(15.2)	(7.0) (70.0)
13 months 4 years	1 (4.0)	5 (10.2)	8 (8.1) (50.0)	2 (5.4)	4 (13.3)	8 (6.5) (40.0)
≥ 5 years	1 (1.2)	4 (6.7)	5 (2.3) (31.2)	2 (2.1)	4 (9.1)	6 (2.4) (30.0)
Total	2 (1.8)	12 (8.2)	16 (4.4)	4 (2.7)	14 (12.7)	20 (4.4)

1. 4 Cases are < 9 months old, and one of them died because of bronchopneumonia.
2. Percentage of hospitalization in certain age-groups among total hospitalization.

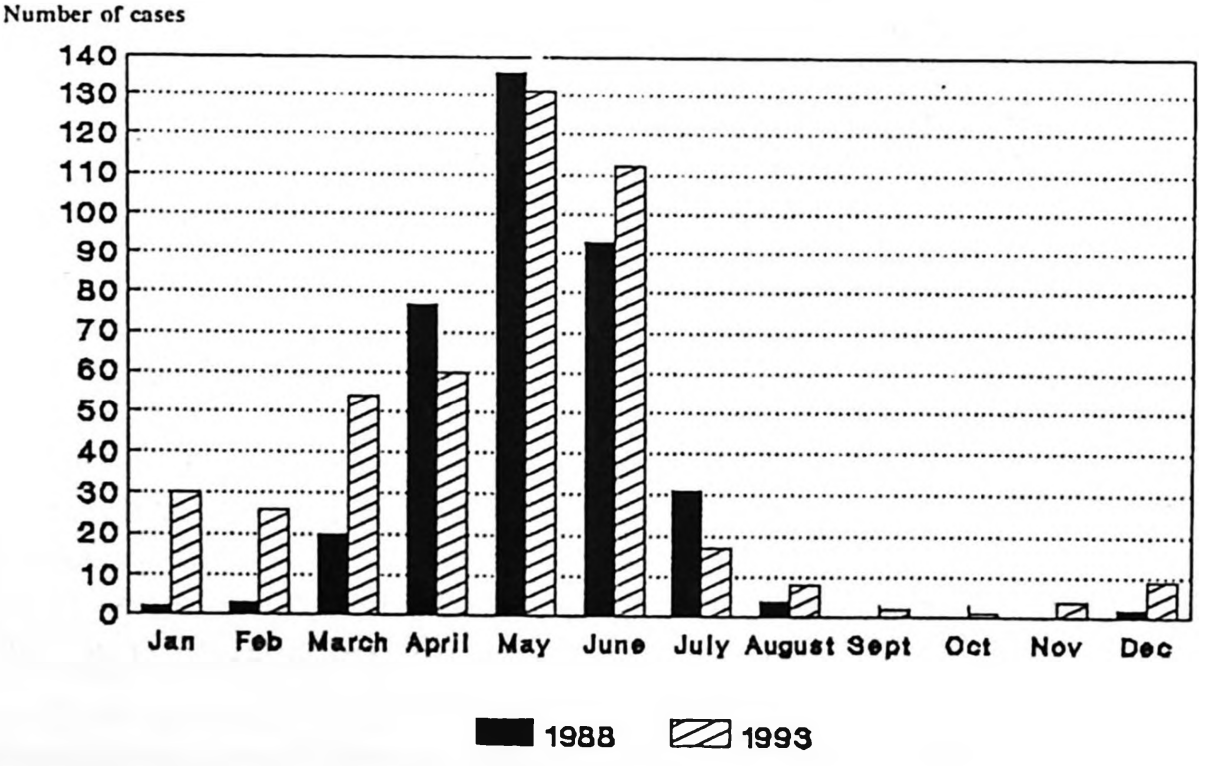

Fig. 3: Distribution of measles cases according to months (1988 and 1993).

Conclusion

The decrease of measles morbidity in our outpatient populations in 1986 and 1987 made us believe in the success of the campaign. During the epidemics of 1983, patients with measles comprised 3.5 percent of all patients in our clinic[10].

In 1986 and 1987 a remarkable decrease (97%) in this rate was observed. Since 1988 (except 1989), a significant increase (412% - 1375%) in measles cases has been seen, a rate which is in agreement with the data of İstanbul Province Health Directorate for the entire city of İstanbul. In spite of the increased rates after 1988, the rates were still lower (66%) than the 1983 rates, even in 1991 when the biggest peak was observed.

The vaccination rate (from 1986 to 1993) for ≤ 5 year-old children was 60-70 percent in İstanbul (data of İstanbul Province Health Directorate). Our data suggest that one of the factors that affected the increase in measles cases was failure to maintain the vaccination rates achieved during the campaign.

When we compared the age distribution of measles cases observed in the epidemics before and after 1985, we noted important differences. In 1983, 70 percent of all measles cases were in children ≤ 4 years of age[10], while after 1985 more than one-half of the measles cases occurred in ≥ 5 years old children. Two results are expected in a partially vaccinated population: a reduction in measles incidence greater than the level of vaccination coverage, and a shift in the age distribution of measles to older children[11-13]. These results are harmonious with our findings.

It is reported that immunization following vaccination after 15 months of age (Schwarz's type) is 95 percent, and the mean rate of primary inefficiency is 5 percent[14]. While only 5 percent or less of appropriately vaccinated children fail to respond, the high transmissibility of measles virus can lead to outbreaks[15-17]. As a result, the Practices Advisory Committee recommends that the second dose of vaccination be administered at the beginning of kindergarten or primary school[18], while the American Academy of Pediatrics recommends a second dose in secondary or high school[19]. When the vaccine is administered to nine-month-old children, the primary inefficiency rate rises to 20 percent[20, 21] and even 31 percent[22] or 37 percent[23]. If we consider Turkey, where vaccination is done routinely at nine months of age and the vaccination rate is around approximately 70 percent, the group at risk is larger and outbreaks can be easily observed. The rule of the cold-chain was not successful until 1985; no problems in the cold-chain were reported after this date[24]. In 1988, 44.7 percent of measles cases were among vaccinated children who were mostly five years old or older, We thought that this was primarily due to cold chain misutilization. In 1993, 57.2 percent of measles cases occurred in vaccinated children, and these cases also

accumulated in the ≥ 5 years group. The reason for this was considered to be the primary inefficiency of the nine-months-old vaccination. As a result, we believed that in both years primary vaccine failure was the cause of measles outbreaks, which mostly occurred in vaccinated children, and the low immunization coverage rates support these outbreaks. The fact that half of the cases observed during the epidemic in Etimesgut, Ankara, occurred among children vaccinated at nine months old[25] supports our thesis.

In the United States, measles epidemics occurring primarily in vaccinated children have been reported[15, 26-28]. During the epidemics of 1989-1990 in the United States, the efficiency of the vaccine was investigated and was found to be approximately 93-98 percent which was similar to rates obtained in previous years. It was also found that vaccine coverage rates among preschool-age children in some cities were 60 percent or lower. According to this data, it was believed that failure to vaccinate rather than vaccine failure was an important cause for the 1989 and 1990 measles epidemics. In this study, it was also demonstrated that 50 percent of the cases were in children under five years old, and 80 percent were unvaccinated although they were of vaccine-eligible age. In our cases, the vaccine efficiency was not investigated, but the rates of children in the < 5-years age-group that were unvaccinated but vaccine-eligible were lower when compared with the rates found in the United States. The incidence of the disease was lower for the unvaccinated younger age groups, and higher for the vaccinated school children in our country when compared with the USA where vaccination is performed routinely beginning at 15 months of age. These results show that vaccination at nine months is beneficial for the young age but becomes a disadvantage as the child grows older.

On the other hand, in 1983 when vaccination was routine after 12-15 months, 27.5 percent of the outpatients and 44 percent of the inpatients were among 0-12-month-old children. After the vaccination age changed to nine months, these rates diminished to 15.1 and 18.8 percent, respectively, in 1988, and 16.7 and 30 percent, respectively, in 1993. During those years, a significant decrease was observed both in rates of mortality and hospitalization compared to 1983. For hospitalization, the rate was shown to be 90 percent reduced in both years, and the mortality rate was shown to be 100 percent reduced in 1988 and 91 percent reduced in 1993. It is obvious that vaccination at nine months diminishes the rate of mortality and morbidity, especially in infants. Although 63 percent immunization provided by vaccination at nine months old carries the benefit of being protective at least until 15 months, these children are under more risk (15%) after the 15th month compared with those vaccinated at 15 months of age.

As a result, and in confirmation of previous studies[15, 29-31] which showed that vaccination before 15 months is a risk factor, we found that it elevated the primary

vaccination inefficiency. Despite this disadvantage of early vaccination, the rates of both mortality and morbidity are diminished, especially in the ≤ 12-month-old age-group. On the other hand, if the vaccination rate is approximately 60-70 percent, an epidemic would not be avoided but its severity would be limited, and the hospitalization and mortality rates would be diminished. If the vaccination rate greater than 80 percent, the incidence decreases significantly. These findings are consistent with those of other researchers[26, 32].

With the information above, we recommend the following to achieve a decrease in epidemics in our country: continuing with the practice of vaccination at nine months, raising the vaccination rates for the first five years and particularly for the first two years, and giving a second opportunity to children who have not been vaccinated or have had primary vaccination inefficiency.

REFERENCES

1. Aaby P. Malnutrition and overcrowding intensive exposure in severe measles infection: review of community studies. Rev Infect Dis 1988; 10: 478-491.
2. Assaad F. Measles: summary of worldwide impact. Rev Infect Dis 1983; 5: 452-459.
3. Borgono JM. Current impact of measles in Latin America. Rev Infect Dis 1983; 5: 417-421.
4. Henderson RH, Keja J, Hayden G, Galazka A, Clements J, Chan C. Immunizing the children of the world: progress and prospects. Bull WHO 1988; 66: 535-543.
5. Ministry of Health of Kenya and World Health Organization. Measles immunity in the first year after birth and the optimum age for vaccination in Kenyan Children. Bull WHO 1977; 55: 21-31.
6. Heymann DL, Mayben GK, Murphy KR, Guyer G, Foster SO. Measles control in Yaounde: justification of a one dose, nine month minimum age vaccination policy in tropical Africa. Lancet 1983; 2: 1470-1472.
7. Tunçbilek E, Ulusoy M, Hancıoğlu A, et al. Hızlandırılmış aşı kampanyası sonrasında 0-5 yaşlarındaki çocukların aşılanma durumu ve kampanya öncesi ile karşılaştırılması. (Nüfusbilim Dergisi) Turk J Popul Stud 1986; 8: 5-35.
8. Uzel N, Sıdal M, Oğuz F, Neyzi O. İstanbul'da 1988 yılında görülen kızamık vakalarının özellikleri. XXXII. Türkiye Milli Pediatri kongresi. 26-28 Ekim, 1988, Ankara. Bildiri Özet Kitabı, 1988: 11.
9. Centers for Disease Control. Classification of measles cases and categorization of measles elimination programs. MMWR 1983; 31: 707-711.
10. Uzel N, Yaka M, Yazıcıoğlu M, Aydoğan Ü. Acil birimine başvuran kızamık vakalarının değerlendirilmesi. İstanbul Tıp Fakültesi VII. Kurultayı. Kurultay serbest bildiri özetleri p. 19, İstanbul, 1983.
11. Dabis F,.Sow A, Waldman RJ, et al. The epidemiology of measles in a partially vaccinated population in an African city: implications for immunization programs. Am J Epidemiol 1988; 127: 171-178.
12. Levy MH, Bridges-Webb C. "Just one shot" is not enough-measles control and eradication. Med J Aust 1990; 152: 489-491.
13. Taylor WR, Mambu RK, ma-Disu M, Weinman JM. Measles control efforts in urban Africa complicated by high incidence of measles in the first year of life. Am J Epidemiol 1988; 127: 788-794.

14. King GE, Markowitz LE, Patriarca PA, Dales LG. Clinical efficacy of measles vaccine during the 1990 measles epidemic. Pediatr Infect Dis J 1991; 10: 883-887.

15. Centers for Disease Control: Measles: United States, 1989 and first 20 weeks. MMWR 1990; 39: 361-363.

16. Brunell PA. Measles vaccine-one or two doses? Pediatrics 1988; 81: 722-724.

17. Gustafson TL, Lievens AW, Brunell PA, Moellenberg RG, Buttery CM, Sehulster LM. Measles outbreak in a fully immunized secondary-school population. N Engl J Med 1987; 316: 771-774.

18. Centers for Disease Control. Measles prevention: recommendations of Immunization Practices Advisory Committee (ACIP). MMWR 1989; 38 (Suppl 9): 1-18.

19. American Academy of Pediatrics. Commitee on Infectious Diseases. Measles: Reassessment of the current immunization policy. Pediatrics 1989; 84: 1110-1113.

20. Berry S, Hernandez H, Kanashiro R, et al: Comparison of high titer Edmonston-Zagreb, Biken-CAM and Schwarz measles vaccines in Peruvian infants. Pediatr Infect Dis J 1992; 11: 822-827.

21. Job JS, Halsey NA, Boulos R, et al. Successful immunization of infants at 6 months of age with high dose Edmonston-Zagreb measles vaccine. Pediatr Infect Dis J 1991; 10: 303-311.

22. Tidjani O, Grunitsky B, Guerin N, et al: Serological effects of Edmonston-Zagreb, Schwarz, and AIK-C measles vaccine strains given at ages 4-5 or 8-10 months. Lancet 1989; 2: 1357-1360.

23. Expanded Programme on Immunization seroconvertion after measles immunization. Wkly Epidemiol Rec 1981; 30: 234-237.

24. The Situation Analysis of Mothers and Children in Turkey, Goverment of Turkey-UNICEF Programme of cooperation. Country Programme, 1991-1995. April 1991; 167-175.

25. Ceyhan M, Kanra G, Vargel S, Işıkçelik Y. The evaluation of vaccination against measles at nine months of age: report of an epidemic. Turk J Pediatr 1992; 34: 127-133.

26. Schlenker TL, Bain C, Baughman AL, Hadler SC. Measles herd immunity: the association of attack rates with immunization rates in preschool children. JAMA 1992; 267: 823-826.

27. Markowitz LE, Preblud SR, Fine PE, Orenstein WA. Duration of live measles vaccine-induced immunity. Pediatr Infect Dis J 1990; 9: 101-110.

28. Grimes DE, Woolbert LF. Measles outbreaks: who are at risk and why. J Pediatr Health Care 1989; 3: 187-193.

29. Mast EE, Berg JL, Hanrahan LP, Wassell JT, Davis JP. Risk factors for measles in a previously vaccinated population and cost-effectiveness of revaccination strategies. JAMA 1990; 264: 2529-2533.

30. Chen RT, Goldbaum GM, Wassilak SG, Markowitz LE, Orenstein WA. An explosive point-source measles outbreak in a highly vaccinated population: modes of transmission and risk factors for disease. Am J Epidemiol 1989; 129: 173-182.

31. McCombie SC, Worrell RD, Porter BW, Browning JA, Ray GG. Risk for measles related to immunization status in two Tucson high schools. Public Health Rep 1988; 103: 162-166.

32. Centers for Disease Control. Progress toward achieving the national 1990 objectives for immunization. MMWR 1988; 37: 613-617.