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Original Article

Prevalence of Protective Measles Virus Antibody Levels in Umbilical Cord Blood Samples and Sera of Mothers and Transplacental Transport Ratio in Turkey

Serap CETIN COBAN[1]*, Fehminaz TEMEL[1] , Pinar DUMAN[1] , Yasemin COSGUN[2], Fatma OZARSLAN[1], Tuba KAYMAN[1], Sirin GUVEN[3],Handan BEZIRGANOGLU[4], Omer GUNES[4], Dilek YILMAZ CIFTDOGAN[5], Ese Eda KARADAGLI[6], Cemil KAYA[6], and Ates KARA[7]

[1]Department of Health Threats Early Warning and Response and [2]Department of Microbiology Reference Laboratories and Biological Products, General Directorate of Public Health, Sağlık Mahallesi, Ankara; [3]University of Health Sciences İstanbul Umraniye Training and Research Hospital, Istanbul; [4]Zekai Tahir Maternity and Child Health Hospital, Ankara; [5]Tepecik Education and Research Hospital, Izmir; [6]Maternity and Child Health Hospital, Sanliurfa; and [7]Children Hospital of Hacettepe University, Ankara, Turkey

SUMMARY: In Turkey, the Measles Elimination Program has been implemented since 2002. The aim of this study was to evaluate the measles-specific antibody levels of mothers admitted to a hospital for birth and their infants, to determine the factors influencing the antibody levels of both, and to evaluate the transplacental transport ratio. We selected healthy women who came to the hospital for birth and their healthy newborns. We collected blood samples from 1,547 mothers and 1,529 infants. The protective prevalence of measles antibody levels of mothers was 80% (95% confidence interval [CI]: 78–82%) and that of newborns was 85% (95% CI: 83–86%). The antibody levels of mothers and newborns were positively linearly correlated (R: 0.922, $p < 0.001$) and were associated with parity ($p < 0.001$). The ratio of neonatal to maternal antibody levels increased with gestational age. The protective levels were 1.6 times higher (95% CI: 1.1–2.4) in mothers ≥ 32 years of age and 2.1 times higher (95% CI: 1.4–3.3) in naturally immune mothers. Two factors affecting the antibody levels of newborns were the mothers' antibody levels and their immunization status. The antibody level of mother was the most significant factor that influenced the infant's antibody level. Vaccination of women before pregnancy could enhance passive antibody protection by increasing the level of transplacental transmission.

INTRODUCTION

Measles is a highly contagious viral disease, primarily transmitted via airborne respiratory droplets from the infected person. Measles is still commonly transmitted worldwide, including some countries in Europe, Asia, the Pacific, and Africa. Despite the presence of a safe and effective vaccine, it is still one of the leading causes of death among children worldwide (1).

The United Nations Millennium Development Goal 4 aimed to decrease the under-five mortality rate by more than half, dropping from 90 to 43 deaths per 1,000 live births between 1990 and 2015. Globally, significant progress has been made in reducing mortality in children under 5 years of age mostly through immunization, and measles vaccination coverage has become a useful indicator of the strength of immunization programs and of child health programs in general. Measles vaccination resulted in an 84% drop in measles deaths between 2000 and 2016 worldwide. During this period, measles vaccination prevented an estimated 20.4 million deaths, making the measles vaccine one of the most effective public health practices (2).

In line with the goals of World Health Organization, the Measles Elimination Program has been implemented since 2002 and the Rubella and Congenital Rubella Syndrome Elimination Program since 2006. The aims of these programs are to eliminate measles and rubella, prevent congenital rubella syndrome, and sustain vaccination coverage levels in Turkey. One of the main immunization strategies of the programs is to sustain at least a 95% vaccination coverage level for 2 measles doses at the district and provincial level (3). Measles was endemic in 2015, but Turkey has interrupted measles transmission for at least 24 months in 2017 (4,5).

In Turkey, monovalent measles immunization started in the 1970s. In 1980, one-dose vaccination was started at 12 to 15 months of age and systematically administered in 1985 with the Expanded Immunization Program. Administration of a second dose to children of 6 years of age was started in 1998. The measles, mumps, and rubella (MMR) vaccine was introduced in 2006. Currently, the MMR vaccine is given at 12 months and again at 6 years of age, with a vaccine coverage level above 90% for the first dose and 85% for the second dose (6).

As a result of these efforts, the number of measles cases in Turkey decreased from 30,509 in 2001 to 34 in 2006, 3 in 2007, and 4 each in 2008 and 2009. The number of confirmed measles cases in Europe increased

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*Corresponding author: Mailing address: Department of Health Threats Early Warning and Response, General Directorate of Public Health, Ministry of Health, Saglik Mahallesi, A. Adnan Saygun Cad, No: 55/D, Sihhiye, Cankaya, Ankara, Turkey. Tel: +90-312-416 82 27, Fax: +90-312-565 54 86, E-mail: serapcobansaglik@gmail.com

to 32,480 (5.87 per 100,000) in 2010 (7). In Turkey, a measles outbreak comprising 111 cases (0.15/100,000) occurred in Istanbul from December 25, 2010 to July 26, 2011. A second outbreak started on January 13, 2012. Until April 2013, the incidence rate was 4.04/100,000 (3,405 cases) (8). Between May 2012 and April 2013, 8,586 measles cases were reported in 30 European countries (9).

During that outbreak, there were cases among infants under 12 months of age, which led to questions of whether the antibodies transferred from mothers to infants do not protect the infants anymore and whether a change in vaccination schedule was needed (8). In recent years, measles cases have increased among infants, especially those under 9 months of age in Turkey. According to measles surveillance data, there were 106 cases in infants under 12 months of age in 2015, zero in 2016, and 26 in 2017. There were no deaths due to measles from 2015 to 2017. Measles can be serious in all age groups, but children younger than 5 years of age are more likely to experience measles complications.

There have been a limited number of studies regarding measles antibody levels in infants and their mothers at birth in Turkey. The first goal of this research was to evaluate the measles-specific antibody levels of mothers admitted to a hospital for birth and their infants and to determine the factors influencing antibody levels. The second goal was to evaluate the transplacental transport ratio of the maternal antibodies.

MATERIALS AND METHODS

Study design and settings: In Turkey, the hospital-birth rate is 97.2% (10). We selected 4 hospitals that had the highest hospital-birth numbers in 4 provinces (Ankara, Istanbul, Izmir, and Sanliurfa) from 4 different regions of Turkey. There were 1,325,783 live births in Turkey in 2015 with the highest number in Istanbul (241,121) followed by Ankara (76,944), Sanliurfa (62,056), and Izmir (55,553) (10). We selected the hospitals according to the following criteria: highest hospital-birth rate in the province, highest rate of regular follow-up, and willingness to volunteer to participate in the study. The Training and Research Hospital Ethical Committee approved the study.

We conducted this study between April 2016 and April 2017 and selected healthy women who came to the hospital for birth and agreed to participate in the study along with their healthy newborns. We calculated the sample size as 1,600 in total: 400 mother-infant pairs for each province. Of 1,591 mothers who agreed to participate in the study, 1,555 completed the questionnaire. We collected serum samples from all pregnant women within 12 h before the birth, and the questionnaire was completed. All participants signed an informed consent before enrollment. The questionnaire included independent variables such as the mother's sociodemographic characteristics (birthdate, birthplace, place of residence, education status, profession, household size, registration with family physician), clinical history (diagnosed diseases, medications used, history of rash, diagnosis of measles), history of vaccination (vaccines administered in childhood and school, bacillus Calmette-Guerin vaccine scar, MMR vaccine history), history and characteristics of previous births, some characteristics of the last pregnancy (smoking status, medication, diseases, vaccines, vitamins used, prenatal care), type of delivery, week of delivery, sex of the newborn, and birth weight. The dependent variables were the measles IgG antibody levels (mIU/mL) of the mother and the newborn.

Immediately after birth, the cord was clipped and cut off, and 5 mL blood samples were collected from the umbilical cord at the site closest to the newborn.

Enrollment of mothers in the study: Healthy Turkish citizens aged 18–49 years were enrolled at 36–42 weeks pregnancy, and those who gave birth at term by spontaneous vaginal delivery or cesarean delivery to an infant with normal birth weight were included in the study.

Mothers were excluded from the study for multiple pregnancy or family history of immune deficiency; infants were excluded for immune deficiency, congenital abnormalities, genetic disease, hematological disorders, birth asphyxia, or congenital heart disease.

Definitions: The age of the mothers was classified according to the measles vaccine administration dates in Turkey. The first group included mothers 26 years of age or younger who were supposed to have been vaccinated twice. The second group was 27–31 years of age who were supposed to have been vaccinated once, and the last group was 32 years of age or older who may not have been vaccinated or had a measles diagnosis.

Healthy mothers were defined as those who did not have diabetes mellitus, autoimmune disease, or a disease requiring blood transfusion or chronic medication or any other clinical condition requiring regular medical follow-up. Regarding education, mothers unable to read and write were defined as illiterate, and those able to read and write but who did not complete primary school were defined as literate. Education was further classified as graduation from primary, secondary, or high school or university. Normal birth weight was defined as birth weight between 2,500 and 4,500 g. Term birth was defined as reaching gestational age of 36–42 weeks.

Because there were no hard copies or electronic health records of measles vaccination for previous years, the mothers' immunization status was classified into 3 groups according to the mothers' statements as follows: (i) naturally immune for mothers with a previous measles diagnosis, (ii) vaccinated for mothers who had received at least one dose of measles vaccine in childhood in school or vaccination campaigns, or (iii) unvaccinated for mothers who had never received a measles vaccine or had the disease.

Regarding protective level, we classified the measles IgG antibody levels of the mothers and the infants as protective for antibody levels > 200 mIU/mL or as unprotective for antibody levels $\leq$ 200 mIU/mL. The ratio of neonatal to maternal antibody levels (neonatal/maternal ratio [NMR]) was calculated as log (neonatal level)/log (maternal level).

Measles antibody analysis: We collected blood samples from 1,547 mothers and 1,529 infants. Samples were centrifuged at 3,500 $\times$ *g* for 15 min, and serum was transferred into a 2mL cryotube in sterile conditions. Samples were stored at –20ºC until transfer (maximum 2 weeks). The serum samples

were transferred on dry ice to the Reference Virology Laboratory of the Ministry of Health in the capital city, Ankara. Serum samples were stored at 80 ºC ± 10ºC after reaching the laboratory. Before the test, the sera were allowed to stand for 1 h and were processed when they reached room temperature.

For the measles IgG antibody analysis, we used the Enzygnost® Anti-Measles Virus/IgG test kit (Siemens, Marburg, Germany). The sensitivity and specificity of the test stated by the manufacturer was 99.6% and 100%, respectively. It is an indirect enzyme-linked immunosorbent assay (ELISA) on a microplate coated with inactivated measles antigen, which is read on an ELISA reader. After the ELISA was performed, the optical density values of the microplates were read in a spectrophotometer at a wavelength of 450 nm.

Results are expressed in corrected absorbance values (ΔA) and classified as negative, equivocal, or positive for assay values < 0.100, ≥ 0.100 to ≤ 0.200, or > 0.200, respectively. A quantitative result can be obtained for samples where the mean absorbance was higher than the limit value (0.100), calculated using the α-method and expressed in mIU/mL. All the techniques were performed following manufacturers' instructions (11).

We performed the quantitative evaluation using the corrected ΔA and kit-lot-dependent α and β using the α-method and the following formula:

$$\text{Log}_{10}\ \text{mIU/mL} = \alpha \times \Delta A^{\beta}$$

$$A = 3.5049 \qquad \beta = 0.2070$$

Statistical analysis: The statistical analysis was performed using the IBM SPSS version 23 (Release 23.0.0.0) software. Statistical significance was defined as $p < 0.05$.

The general characteristics of mothers and infants are given for 1,555 mothers, and further analyses were performed on 1,547 mothers and 1,529 infants who had provided blood samples. As the antibody levels were not normally distributed, we used nonparametric tests (Chi-square, Mann-Whitney U, Kruskal-Wallis) to compare the groups. Antibody data were log transformed and geometric mean (GM) titers (95% confidence interval [CI]) were used to compare groups. We analyzed the proportion of both mothers and infants with protective measles antibody levels. The correlation of antibody levels of mothers and infants was evaluated using linear regression.

We built 2 logistic regression models. The first model was to determine the possible indicators of antibody levels in mothers and included mother's age, history of measles diagnosis, immunization status, and parity. The outcome variable was the protective levels of mothers (protective/unprotective). The second model was for newborns and included antibody levels and immunization status of the mothers. The outcome variable was the protective levels of infants (protective/unprotective). The factors that were not associated with the antibody levels in a previous analysis were not included in the models. Interactions and confounding factors were explored.

Ethical approval: We obtained the ethical approval from the local Training and Research Hospital Ethical Committee (Approval no. E-14-243/2014).

RESULTS

Characteristics of the study population: The general characteristics of mothers and newborns are given in Table 1. Among the mothers, 47.8% were ≤ 26 years old, 12.3% were illiterate, and 29.6% had graduated from primary school. The average household size was 5 ± 2 persons.

According to self-reports of mothers, 10.2% had a previous measles diagnosis, 73.5% received at least one dose of measles vaccine, and 10.1% were unvaccinated.

Mean parity was 2.4 ± 1.4 and the first gestational age was 18–35 years in 89.6% of mothers. The rate of vaginal delivery was 63%, and 52% of the newborns were male. The mean birth weight of newborns was 3,299 ± 415 g (Table 1).

Serological results of mothers and newborns: The protective prevalence of measles antibody levels of mothers was 80% (95% CI: 78–82%) and that of the newborns was 85% (95% CI: 83–86%). The measles antibody levels of mothers ≥ 32 years of age and that of their newborns were higher ($p < 0.001$). Antibody levels were higher in illiterate, literate, and university graduate mothers and their children ($p < 0.001$) and in mothers and children who lived in crowded houses ($p < 0.001$). Antibody levels were highest in naturally immune mothers (GM: 2,033), and their infants (GM: 2,450), and mothers who gave birth via vaginal delivery ($p < 0.001$) (Table 2).

Seventy-five percent of mothers of the infants who had unprotective antibody levels at birth were ≤ 26 years of age, and 80% stated that they were vaccinated with at least one dose. The antibody levels of these mothers were responsible for only 23.3% of the low levels in infants (data not shown). The antibody levels of mothers and newborns were not associated with gestational week or birth weight ($p > 0.05$) but were associated with parity ($p < 0.001$) (Table 2).

There was a strong, positive linear correlation between the antibody levels of mothers and newborns (R: 0.922, $p < 0.001$) (Fig. 1). The NMR was 1.07 in mothers with unprotective levels of antibodies, 1.02 in those with protective levels, and 1.03 overall (Table 3).

Fig.2 shows the transplacental transport ratio according to mothers' age and gestational age. In every age group, the NMR increased with gestational age (Fig. 2).

Model-based analysis: In the model constructed for evaluating possible indicators of antibody levels of mothers, after controlling other factors, protective levels were 1.6 times higher (95% CI: 1.1–2.4) in mothers ≥ 32 years of age and 2.1 times higher (95% CI: 1.4–3.3) in naturally immune mothers. It was 2.6 times higher (95% CI: 1.5–4.5) in mothers who had 4 or more children and 1.6 times higher (95% CI: 1.1–2.3) in mothers who had 3 children (Table 4).

The other model for newborns showed that there were 2 factors that affected the antibody levels of infants: the antibody level of the mother and the immunization status of the mother. Each 1 mIU/mL increase in the antibody levels of mothers caused an increase of 1.019 mIU/mL in the infants' level (95% CI: 1.016–1.023 mIU/mL) (Table 4).

Table 1. Characteristics of mothers and newborns

Characteristics of mothers		*n*	%
Age (yr) (*n* = 1,553)	≤ 26	742	47.8
	27 – 31	429	27.6
	≥ 32	382	24.6
	Mean ± SD: 27.5 ± 5.7	Median:27.0	Min-Max: 18–46
Education (*n* = 1,541)	Illiterate	189	12.3
	Literate	113	7.3
	Primary school	456	29.6
	Secondary school	402	26.1
	High school	266	17.3
	University	115	7.5
Household size (*n* = 1,555)	1 – 4	773	49.7
	5 – 8	669	43.0
	9 – +	113	7.3
	Mean ± SD: 5.0 ± 2.0	Median: 5.0	Min-Max: 2–19
Immunization status (*n* = 1,545)	Naturally immune	158	10.2
	Vaccinated	1,135	73.5
	Unvaccinated	156	10.1
	Unknown	96	6.2
First gestational age (*n* = 1,553)	< 18	146	9.4
	18–35	1,392	89.6
	> 35	15	1.0
	Mean ± SD: 22.2 ± 4.2	Median: 21.0	Min-Max: 13–42
Number of pregnancies (*n* = 1,554)	1	488	31.4
	2	494	31.8
	3	337	21.7
	4 +	235	15.1
	Mean ± SD: 2.4 ± 1.4	Median: 2.0	Min-Max: 1–10
Characteristics of the last pregnancy			
Smoking status (*n* = 1,553)	Yes	172	11.1
	No	1,381	88.9
Immunization against tetanus (*n* = 523)	Yes	114	73.7
	No	344	22.2
	Unknown	65	4.2
Vitamin D supplementation (*n* = 1,491)	Yes	743	49.8
	No	694	46.5
	Unknown	54	3.6
İron supplementation (*n* = 1,540)	Yes	1,206	78.3
	No	289	18.8
	Unknown	45	2.9
Folic acid supplementation (*n* = 1,516)	Yes	678	44.7
	No	766	50.5
	Unknown	72	4.7
Type of delivery (*n* = 1,552)	Vaginal	980	63.1
	Caesarean	572	36.9
Characteristics of the newborn		*n*	%
Sex (*n* = 1,553)	Male	808	52.0
	Female	745	48.0
Gestational age (week) (*n* = 1,553)	36	44	2.8
	37	138	8.9
	38	412	26.5
	39	504	32.5
	40	349	22.5
	41	94	6.1
	42	12	0.8
	Mean ± SD: 38 weeks 6 days	Median:39 weeks	Min-Max:36–42
Birth weight (gr) (*n* = 1,551)	< 2,500	29	1.9
	2,500–3,499	1,031	66.5
	3,500–4,499	476	30.7
	> 4,500	15	1.0
	Mean ± SD: 3,299 ± 415	Median: 3,250	Min-Max: 1,860–5,034

Table 2. Measles antibody levels and prevalence of protective levels of mothers and newborns at birth (GM, mIU/mL)

	Mothers					Newborns				
	n	GM (95% CI)	*p*	% Protective	*p*	*n*	GM (95% CI)	*p*	% Protective	*p*
Age (yr)										
≤ 26	724	709 (626–797)	< 0.001	74 (71–78)	< 0.001	712	883 (790–988)	< 0.001	81 (78–84)	< 0.001
27–31	414	1,125 (957–1,330)		82 (78–86)		412	1,374 (1,164–1,627)		86 (82–89)	
≥ 32	372	1,537 (1,301–1,797)		87 (83–90)		369	1,819 (1,539–2,126)		90 (87–93)	
Education										
İlliterate	174	2,300 (1,849–2,852)	< 0.001	93 (89–97)	< 0.001	171	2,635 (2,074–3,308)	< 0.001	94 (91–98)	< 0.001
Literate	100	1,721 (1,188–2,502)		83 (76–90)		102	1,996 (1,483–2,713)		90 (84–96)	
Primary School	454	1,102 (940–1,283)		81 (77–84)		450	1,294 (1,100–1,516)		85 (81–88)	
Secondary School	396	663 (563–800)		72 (68–77)		384	821 (697–969)		79 (75–83)	
High School	264	669 (554–819)		77 (71–82)		264	895 (742–1,070)		83 (79–88)	
University	112	871 (650–1,176)		83 (76–90)		112	1,127 (851–1,482)		88 (81–94)	
Household size										
1–4	760	750 (662–848)	< 0.001	75 (72–78)	< 0.001	753	970 (866–1,084)	< 0.001	82 (79–84)	0.008
5–8	647	1,179 (1,038–1,339)		84 (81–87)		636	1,361 (1,198–1,541)		87 (85–90)	
9–+	104	1,969 (1,432–2,672)		85 (78–92)		105	2,337 (1,726–3,150)		88 (81–94)	
Immunization status										
Naturally immune	158	2,033 (1,570–2,623)	< 0.001	89 (84–94)	0.001	154	2,450 (1,900–3,116)	< 0.001	94 (90–97)	< 0.001
Vaccinated	1,121	810 (726–894)		77 (75–80)		1,107	988 (896–1,097)		82 (80–84)	
Unvaccinated	151	1,141 (869–1,461)		83 (77–89)		151	1,430 (113–1,836)		87 (81–92)	
Unknown	80	2,123 (1,449–2,992)		89 (82–96)		81	2,745 (1,940–3,704)		96 (92–100)	
Type of delivery										
Vaginal	941	1,085 (974–1,214)	0.001	81 (79–84)	0.024	937	1,363 (1,223–1,512)	< 0.001	87 (84–89)	0.005
Caesarean	568	810 (699–934)		77 (73–80)		556	947 (827–1,092)		81 (78–84)	
Gestational age (week)										
36	43	708 (415–1,216)	0.239	77 (64–90)	0.055	43	762 (440–1,279)	0.453	79 (66–92)	0.235
37	131	1,188 (891–1,581)		84 (78–90)		131	1,344 (1,015–1,779)		89 (84–95)	
38	389	1,095 (919–1,300)		81 (77–85)		385	1,302 (1,101–1,529)		85 (81–89)	
39	492	977 (840–1,130)		82 (78–85)		487	1,194 (1,035–1,372)		85 (81–88)	
40	349	850 (696–1,026)		73 (69–78)		343	1,087 (908–1,303)		81 (77–85)	
41	94	901 (634–1,270)		83 (75–91)		93	1,237 (882–1,698)		89 (83–96)	
42	12	640 (258–1,424)		83 (59–100)		12	911 (362–1,868)		92 (73–100)	
Birth weight (gr)										
< 2,500	29	688 (319–1,407)	0.279	76 (59–92)	0.969	28	744 (377–1,463)	0.207	79 (62–95)	0.745
2,500–3,499	1,003	966 (866–1,074)		80 (77–82)		993	1,193 (1,087–1,324)		85 (83–87)	
3,500–4,499	461	974 (835–1,145)		80 (76–83)		458	1,196 (1,022–1,389)		84 (81–87)	
≥ 45,00	15	2,107 (837–5,385)		80 (57–100)		15	2,348 (814–5,561)		80 (57–100)	
Parity										
1	474	628 (528–724)	< 0.001	72 (68–76)	< 0.001	466	828 (711–955)	< 0.001	79 (75–83)	< 0.001
2	487	949 (815–1,089)		80 (76–83)		482	1,149 (985–1,328)		84 (81–88)	
3	331	1,092 (923–1,305)		83 (79–88)		327	1,275 (1,070–1,548)		87 (83–91)	
4+	219	2,228 (1,815–2,681)		90 (86–94)		219	2,530 (2,043–3,069)		93 (89–96)	
Total	1,547	962 (884–1,045)		80 (78–82)		1,529	1,182 (1,078–1,278)		85 (83–86)	

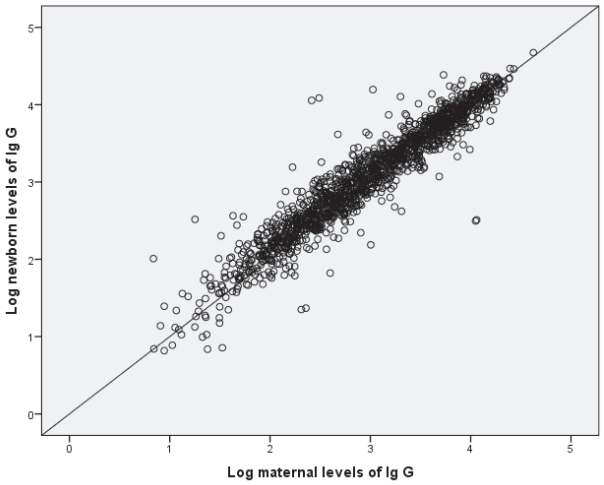

Fig. 1. Regression line of log newborn and maternal levels of measles IgG.

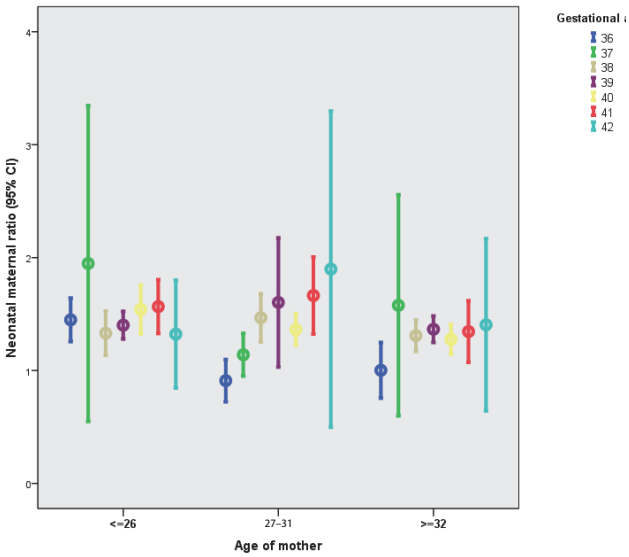

Fig. 2. (Color online) Transplacental transport ratio by mothers' age and gestational age.

Table 3. Geometric mean concentration (GMC) of measles antibodies and neonatal maternal ratio in mother-infant pairs by protective level

Protective level of mothers at birth	*n*	Maternal serum	Neonatal serum	Neonatal Maternal Ratio
		GMC (95% CI)	GMC (95% CI)	
Unprotective	310	84 (78–91)	119 (108–131)	1.07
Protective	1,214	1,795 (1,670–1,926)	2,116 (1,977–2,267)	1.02
Overall	1,524	963 (882–1,051)	1,178 (1,083–1,281)	1.03

Table 4. Logistic regression models for possible indicators of protective levels in mothers and infants

Possible indicators of protective levels in mothers (n = 1,509)	OR_{adj} (95% CI)	Wald test p
Age of mothers		
≥ 32	1.6 (1.1 – 2.4)	0.015
27 – 31	1.3 (1.0 – 1.8)	0.087
≤ 26 (ref)	1	–
Immunization status		
Naturally immune	2.1 (1.4 – 3.3)	0.001
Unvaccinated	1.3 (0.8 – 2.0)	0.353
Vaccinated (ref)	1	–
Parity		
≥4	2.6 (1.5 – 4.5)	0.001
3	1.6 (1.1 – 2.3)	0.021
2	1.4 (1.1 – 1.9)	0.023
1 (ref)	1	–
Possible indicators of protective levels in Infants (n = 1488)		
Immunization status		
Naturally immune	2.5 (1.1 – 5.9)	0,034
Unvaccinated	0.8 (0.3 – 1.9)	0.798
Vaccinated (ref)	1	–
Antibody level of mothers (mIU/mL)		
1 mIU/mL increase in antibody levels of mothers	1.019 (1.016 – 1.023)	< 0.001

DISCUSSION

This study, which aimed to evaluate the measles IgG antibody levels of mothers and newborns at birth, is the most comprehensive study in this area in Turkey. We achieved important results regarding public health implementations.

In Turkey, in 2 outbreaks of measles that were seen in recent years, most of the patients were infants younger than 12 months. The limited number of studies in this area made it difficult to decide whether there was a problem with the transfer of antibodies from mothers to newborns. Despite the fact that studies in other parts of the world showed that antibody levels of mothers are decreasing in highly vaccinated populations due to vaccine-induced immunity, we did not know if it was also true for Turkey (12). There were a limited number of local studies (13–16). This study provided scientific evidence to examine this phenomenon for Turkey and made it possible to compare the results with other countries. In the last decade, measles vaccine coverage was greater than 90% in Turkey (17). As measles vaccine coverage increases, it is essential to identify the risk factors for measles and target risk groups for supplementary immunization strategies (18). This study also filled the gap on research for evidence-based decisions on measles vaccination strategies in Turkey. Measles seroprevalence should be reevaluated periodically as the local and global measles epidemiology changes (19).

We found that the antibody level of the mother was the most significant factor that influenced the infant's antibody level. The passive immunization in infants achieved by maternal antibodies depends on 4 factors: maternal antibody levels, effective transplacental transmission of IgG antibodies, gestational age, and decay rate of the antibody levels (20). This means that if we can increase the antibodies in mothers, we can also increase the antibody levels in infants. One of the most important possible indicators of maternal antibody levels was the mother's age, which reflects the vaccine administration schedule in Turkey. The older mothers who had previously had measles transferred more antibodies to their newborns than the other mothers. As vaccine coverage levels in these birth cohorts in Turkey ranges from 30% in 1986 to 80% in 1999, the mothers eligible for one dose of vaccine had a higher prevalence of protective antibody than those eligible for 2 doses of vaccine.

Studies have shown that naturally immune mothers could transfer more antibodies to their newborns than the vaccinated or unvaccinated mothers (21,22). Gans and colleagues recommend vaccinating women of childbearing age before pregnancy or using vaccines that are safe for administration during pregnancy (23). Zhao and colleagues suggested offering an additional measles vaccination for women before pregnancy so that their future infants could get more maternal measles IgG and have a longer duration of protection against measles (24). This strategy has been implemented previously for other vaccine-preventable diseases such as polio and neonatal tetanus (25). We also think that it could enhance passive antibody protection through increasing transplacental transmission of IgG antibodies. Mothers who gave birth by vaginal delivery had higher antibody levels, and this finding cannot be explained by biological mechanisms. We could not find any research results that support this finding (26). Parity was also found to be associated with the antibody results, possibly owing to collinearity by age.

The prevalence of protective levels in newborns at birth indicates that nearly 20% might not be protected from the disease at birth. Transplacental transmission is influenced by coinfections, malnutrition, and vaccine coverage in the country (21,27). In this study we found that the mother's age and gestational age affected the transmission of antibodies. Studies show that prematurity also influences this transmission (28–30), which is why we excluded premature babies from our study. The transplacental transport ratio changed with gestational age in our study. This ratio was higher in infants of 40 and 41 weeks gestational age. There are studies showing that the gestational age and the antibody levels increase in correlation. Perinatal care also needs to be improved to reduce the risk of preterm birth.

We could not obtain vaccination records or the history of measles diagnosis of mothers, as there were no electronic health records and the diagnosis was mostly clinical in the past. Since the elimination program has been implemented, all of the samples need to be confirmed by reference laboratories and multiple questions were included in the questionnaire to check this information. The selection of the hospitals with high birthrates may have caused a selection bias.

In conclusion, this study achieved important results regarding antibody levels of mothers and newborns at birth. We also invited mothers and their infants to participate in a follow-up study in the future to provide information on decay rates. We wrote a report including our results and recommendations to be discussed at the Vaccine Advisory Board of the Ministry of Health. In highly vaccinated populations such as in Turkey, health professionals should recommend additional vaccine schedule strategies. We also think that we need a plan for new vaccine administration schedules especially for women preparing for pregnancy.

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Conflict of interest None to declare.

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