

Prevalence of toxoplasma, cytomegalovirus and rubella in pregnant women in Erzurum, Turkey

Ahmet Yilmaz¹, Mahmut Ucar²

¹Department of Clinical Microbiology, Vocational School of Health Services, Ataturk University, Erzurum, Turkey

²Department of Medical Microbiology, Faculty of Medicine, Ataturk University, Erzurum, Turkey

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Abstract

Aim: In this study, the seroprevalence of IgM- and IgG- type antibodies against Toxoplasma, Cytomegalovirus (CMV) and Rubella virus was investigated in pregnant women with routine controls performed by family physicians in the city center of Erzurum in a two-year period. It was aimed to compare the obtained data with other studies conducted in our country and in the world.

Materials and Methods: The specific results of IgM and IgG serology of Toxoplasma, CMV and rubella of 6798 pregnant women performed by family physicians in the city center of Erzurum between 01.01.2018 and 31.12.2019 were investigated and evaluated according to different age groups in this retrospective cross-sectional study. The serum samples were studied using the Architect i2000 systems with the Chemiluminescent Microparticle Immunoassay (CMIA) method in Erzurum Public Health Microbiology Laboratory.

Results: The data of 6798 people between the ages of 15-50 were reached in our study. Toxoplasma, Rubella and CMV- (n = 6586) specific IgM antibody seropositivity rates were found as 0.5%, 0.3% and 0.6%, respectively, while Toxoplasma-, Rubella- and CMV-specific IgG antibody seropositivity rates were found as 20.9%, 88.3% and 99.2%, respectively. Toxoplasma IgG seropositivity rates were determined to increase in parallel with increasing age. Rubella IgG seropositivity rates were decreasing in the 15-24, 25-34 and 35-49 age groups, respectively. The lowest Toxoplasma IgM and CMV IgM seropositivity rates were found in the 35-49 age groups.

Conclusions: The two-year seroprevalence of Toxoplasma, CMV and Rubella was determined in pregnant women in our region with this study. Although these seroprevalence rates in Erzurum are generally compatible with other studies conducted in our country, Toxoplasma IgM and rubella IgG seropositivity rates were found to be lower compared to the overall incidence of our country.

Keywords: Cytomegalovirus; pregnant; rubella; seroprevalence; *toxoplasma gondii*

INTRODUCTION

Toxoplasma gondii, *Cytomegalovirus* (CMV), *Rubella* and *Herpes simplex* infections are evaluated together since they cause similar clinical pictures in the fetus when exposed during pregnancy (1). Although the infections caused by these infectious agents, also known as the TORCH group, are mostly asymptomatic diseases that can be observed in most segments of the society and in all age groups, they are quite important since they cause congenital malformations in the fetus if pregnant women get infected as a result of contact with these factors, especially in the first trimester (2,3). The prevalence of TORCH infections varies among countries, regions and ethnic groups (4). Many studies conducted in different regions of Turkey report that seropositivity varies depending on the region and special emphasis is placed on seropositivity among different countries (5). Detection of specific IgM antibodies in the early stages of these

infections is a very important approach (6). While IgM-type antibodies against Toxoplasma, CMV and Rubella virus are evaluated as primary infection or recurrent infection, IgG-type antibodies are interpreted as the indicator of past infection. IgM-type antibodies may either become negative after the formation of IgG-type antibodies or remain positive for a long time (2).

The aim of this study is to investigate the seroprevalence of IgM- and IgG-type antibodies against Toxoplasma, CMV and rubella virus in pregnant women with routine controls performed by family physicians between the years of 2018 and 2019, and to compare the results of our province with the studies (seroprevalence studies) conducted in Turkey and in other parts of the world.

MATERIALS and METHODS

In this study, Toxoplasma, CMV and Rubella serology results of 6798 pregnant women in the childbearing

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Corresponding Author: Ahmet Yilmaz, Department of Clinical Microbiology, Vocational School of Health Services, Ataturk University, Erzurum, Turkey E-mail: aymet25@hotmail.com

age who applied to family physicians in the city center of Erzurum between 01.01.2018-31.12.2019 were evaluated retrospectively. The data were obtained from the laboratory automation system. The first evaluation result was taken into consideration in the event of multiple results of the same patient. Toxoplasma IgM was studied in 6619, Toxoplasma IgG was studied in 6542, CMV IgM was studied in 6586, CMV IgG was studied in 3873, rubella IgM was studied in 6629, and rubella IgG was studied in 6533 of the patients included in our study group. Pregnant women in the study group were divided into different age groups as the 15-24, 25-34 and 35-49 age groups in order to make comparisons. The serum samples were studied with the Architect i2000 (Abbott Laboratories, USA) systems using the Chemiluminescent Microparticle Immunoassay (CMIA) method and Architect kit in accordance with the operational procedure of the manufacturer in Erzurum Public Health Microbiology Laboratory where internal and external quality controls were regularly performed. The results were evaluated as negative, intermediate and positive values based on the cut-off values of the kit manufacturer. According to the instructions of the kit manufacturer, a value of <0.5 was considered as the negative index value, a value between 0.5-0.6 was considered as the intermediate index value, and a value of >0.6 was considered as the positive index value for Toxoplasma IgM; while a value of <1.6 IU/ml was considered as the negative result, a value between 1.6-2.99 IU/ml was considered as the intermediate result, and a value of >2.99 IU/ml was considered as the positive result for Toxoplasma IgG. A value of <0.85 was considered as the negative index value, a value between 0.85-0.99 was considered as the intermediate index value, and a value of >0.99 was considered as the positive index value for

CMV IgM; while a value of <5.99 AU/ml was considered as the negative result, and a value of >5.99 AU/ml was considered as the positive result for CMV IgG. A value of <1.2 was considered as the negative index value, a value between 1.2-1.599 was considered as the intermediate index value, and a value of >1.599 was considered as the positive index value for rubella IgM; while a value of <5 IU/ml was considered as the negative result, a value between 5-9.99 IU/ml was considered as the intermediate result, and a value of >9.99 IU/ml was considered as the positive result for rubella IgG. IgM antibodies with intermediate and positive values for all three factors in the first study were re-studied with new serum samples. SPSS 22.0 package program was used in the statistical evaluation of the results. Descriptive data was presented as standard deviation, mean and percentage. Categorical data was analyzed by the chi-square test. A p value of <0.05 was considered statistically significant

Ethics Committee Approval

This study was approved by the Clinical Research Ethics Committee of Ataturk University, Faculty of Medicine (2019/20).

RESULTS

The data of 6798 people were reached in our study. The mean age of pregnant women was 28.3 ± 6.3 years (range, 15-50 years). 6619 serum samples were studied for toxoplasmosis, 6586 serum samples were studied for CMV, and 6629 serum samples were studied for Rubella virus. In our study, Toxoplasma IgM and IgG antibody seropositivity rates were 0.5% and 20.9%, respectively. CMV IgM and IgG seropositivity rates were 0.6% and 99.2%, respectively. Rubella IgM and IgG seropositivity rates were 0.3% and 88.3%, respectively (Table 1).

Table 1. Two-year (2018-2019) Toxoplasma. Rubella and CMV IgG and IgM serology results in pregnant women in Erzurum

	15-24 N (%)	25-34 N (%)	35-49 N (%)	Total	p value
T. gondii IgM					
Positive	9 (0.4)	20 (0.6)	3 (0.3)	32 (0.5)	0.208
Negative	1996 (99.3)	3454 (99.3)	1126 (99.7)	6576 (99.4)	
Grayzone	6 (0.3)	5 (0.1)	0 (0)	11 (0.2)	
T. gondii IgG					
Positive	306 (15.4)	719 (20.9)	1234 (34.3)	1369 (20.9)	p<0.05
Negative	1666 (83.7)	2644 (77.0)	731 (65.4)	5041 (77.1)	
Grayzone	19 (1.0)	71 (2.1)	42 (3.8)	132 (2.0)	
CMV IgM					
Positive	14 (0.7)	23 (0.7)	5 (0.4)	42 (0.6)	0.606
Negative	1980 (98.9)	3408 (98.6)	1114 (98.9)	6502 (98.8)	
Grayzone	8 (0.4)	24 (0.7)	7 (0.6)	39 (0.6)	
CMV IgG					
Positive	1206 (98.9)	2029 (99.3)	605 (99.3)	3840 (99.2)	0.131
Negative	11 (0.9)	14 (0.7)	4 (0.7)	29 (0.7)	
Grayzone	3 (0.2)	0 (0)	0 (0)	3 (0.1)	

Rubella IgM					
Positive	6(0.3)	12(0.3)	3(0.3)	21(0.3)	
Negative	1993(99.0)	3455(99.2)	1117(98.7)	6565(99.0)	0.327
Grayzone	14(0.7)	17(0.5)	12(1.1)	43(0.6)	
Rubella IgG					
Positive	1789(90.5)	3082(89.6)	900(80.6)	5771(88.3)	
Negative	94(4.8)	165(4.8)	108(9.7)	367(5.6)	P<0.05
Grayzone	93(4.7)	194(5.6)	108(9.7)	395(6.0)	

The distribution of the seropositivity rates of Toxoplasma/CMV/rubella IgM and IgG antibodies by age groups are shown in Figure 1.

Although, Toxoplasma IgM seropositivity rate was higher in the 25-34 age group compared to other age groups, this was not statistically significant ($p>0.05$). Toxoplasma IgG seropositivity rates were determined to increase in parallel with increasing age. This difference between the age groups was found statistically significant ($p<0.05$). Rubella IgG seropositivity rates were decreasing in the 15-24, 25-34 and 35-49 age groups, respectively, and this difference was statistically significant ($p<0.05$). The differences of CMV IgM and IgG seropositivity rates between the age groups were not found statistically significant ($p>0.05$) (Table 1). While CMV IgM seropositivity rate was slightly lower in the 35-49 age group, there was no significant difference between other age groups ($p>0.05$).

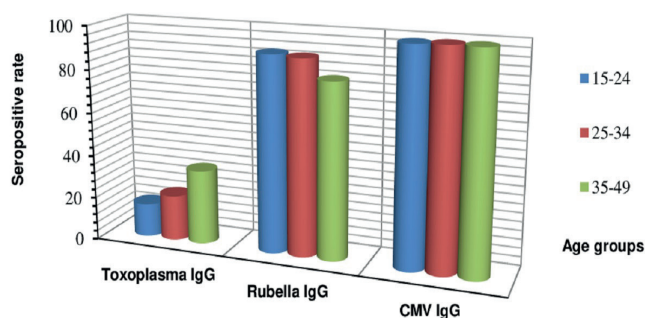


Figure 1. Toxoplasma, Rubella and CMV IgG seropositivity rates in three different age groups

DISCUSSION

Intrauterine infections during pregnancy are of great importance since they cause congenital malformations in the fetus. While discussing the necessity of routine screening to reveal the presence of Toxoplasma, CMV and Rubella infections in pregnant women, it is also necessary to know the seropositivity rates in different regions (2). The prevalence of these infections shows regional differences in pregnant women (6). In line with this aim, we hoped to contribute to the literature in this regard by revealing the seroprevalence of *T. gondii*, CMV and Rubella among pregnant women in our region. The frequency of Toxoplasmosis, which is a very common disease in our country and in the world, may differ depending on many

factors such as the geographical location of the person, hygienic conditions, dietary habits, living conditions, age and frequency of contact with cats. The fact that it causes preterm delivery or even abortion in pregnant women and congenital toxoplasmosis in the neonates brings a correct and early diagnosis of the disease into prominence (7,8). When looking at the studies examining toxoplasma serology of pregnant women in Turkey, Inci et al.(1) found Toxoplasma IgM and IgG seropositivity rates as 1.3% - 18.3% in Artvin, Obut et al.(9) 1.1% - 34.9 in Diyarbakir, Sirin et al.(6) 1.9% - 32.3% in Izmir, Mumcuoglu et al.(10) 0.2% - 6.9% in Ankara, Toklu et al.(2) 3.0% -18.3% in Usak and Tanriverdi et al.(11) 0.6% - 31% in Erzurum.

When examining some studies conducted in pregnant women around the world, Ahmedpoor et al.(12) found Toxoplasma IgM and IgG seropositivity rates as 5.7% - 25.0 in Iran, El-Deeb et al.(13) 2.8% - 67.5% in Egypt, Sahu et al.(14) 1.5% - 39.5% in India, and Alghamdi et al.(15) 6.4% - 32.5 in Saudi Arabia. In our study, Toxoplasma IgM and IgG seropositivity rates were 0.5% - 20.9%. The results were highly compatible with the data of the studies conducted in Turkey. Studies are available reporting that there is a difference between age groups in terms of Toxoplasma seropositivity and an increase is observed in seropositivity rates with increasing age (16,17). Similarly, Toxoplasma IgG seropositivity rates in our study increased with increasing age in parallel with the literature. On the other hand, it is important to provide training on the routes of transmission of Toxoplasma infection and ways to prevent disease, especially for women of childbearing age since Toxoplasma IgG seronegativity rate is as high as 77.1%. Toxoplasma IgM seropositivity rate was found as 0.5% in our study, which is lower than the overall incidence of our country. The low rate of IgM seropositivity might be attributed to the difference in dietary habits especially in our region. In addition, our study is limited to our province and, thus, can be evaluated as an example of regional differences. When compared to a prior study carried out in Erzurum by Tanriveri, although toxoplasma IgM results were similar, toxoplasma IgG results were markedly difference.

It is highly likely that this difference observed in IgG results was resulted from different patient portfolio. Our patient portfolio consisted of people who lives in city centre; however, the patient portfolio of the other research group consisted of district and neighbouring provinces in addition to city centre.

CMV is reported to be the most common cause of congenital viral infections, with a rate of 0.2% - 2.5% of all live births in the world (18,19). The seroprevalence of CMV infections is highly associated with socioeconomic status, poor hygienic conditions or crowded living conditions (20). There are many studies in the literature reporting that CMV seroprevalence rates in developed countries are lower compared to those in developing countries (6). When looking at CMV IgM and IgG seropositivity rates of pregnant women in some studies conducted in our country, Kan et al. (21) found them as 1.8% - 96.4% in Ankara, Obut et al.(9) 0.7% - 99.2% in Diyarbakir, Madendag et al.(5) 0.2% - 98.2% in Kayseri, Inci et al.(1) 1.5% - 98.9% in Izmir, and Toklu et al.(2) 1.0% - 99.4% in Usak. When examining the studies on CMV IgM and IgG seropositivity rates of pregnant women around the world, Zhang et al. (18) found them as 0.9% - 98.7% in China, Enders et al. (22) found CMV IgG as 42.3% in Germany, Pembvey et al. (23) found CMV IgG as 48.4% in England, Sahu et al. (14) found them as 9.5% - 64.9% in India, Alvarado-Esquivel et al. (24) found them as 0% - 89.6% in Mexico, and Pradhan (25) found them as 17.4% - 58.7% in Nepal. In our study, CMV IgM and IgG seropositivity rates were 0.6% - 99.2%. The results were similar to the studies reported in our country. The presence of high seropositivity rates compared to developed countries is related to socioeconomic conditions, and this situation is stated to may be related to crowded living of the families in our region as well as not being able to provide adequate hygienic conditions. It is important to provide seronegative pregnant women with hygiene training to prevent CMV infection in order to reduce the rate of maternal CMV infection during pregnancy.

Rubella is a mild viral infection that typically occurs in childhood, but primary infection during pregnancy results in congenital rubella syndrome (26). Rubella infection usually occurs without any clinical symptoms; therefore, the diagnosis of infection is evaluated by serological evidence (19). When looking at the studies on Rubella in pregnant women in our country, Inci et al.(1) found Rubella IgM and IgG seropositivity rates as 1.2% - 93.5% in Izmir, Obut et al.(9) 0.1% - 94.1% in Diyarbakir, Gurlek et al. (27) 0.9% - 90.7% in Rize, Bakacak et al.(8) 0.2% - 99.3% in Kahramanmaras, and Madendag et al.(5) 0.6% - 97.3% in Kayseri. When examining the studies in pregnant women around the world, Roomande et al.(28) found Rubella IgM and IgG seropositivity rates as 0% - 86.5% in Iran, Muliyl et al. (29) 1.3% - 83.4% in India, Taku et al.(30) 5.0% - 94.4% in Cameroon, and Alvarado-Esquivel et al.(31) 0% - 97.1% in Mexico. In our study, Rubella IgM and IgG seropositivity rates were 0.3% - 88.3%. When the results were compared with other study results in our country, IgG seropositivity rate was especially lower. The decrease in rubella IgG seropositivity with increasing age was statistically significant. Vaccination programs were also thought to be effective in the highest rate of Rubella antibody seropositivity in the 15-24 age groups. Rubella vaccine has been included in the National Immunization Program in our country since 2006 (32).

LIMITATIONS

This is a single-center study and is limited due to its retrospective nature. Therefore, no information was obtained about variables such as vaccination status, living conditions, socioeconomic status and dietary habits of the patients. In addition, the avidity test results could not be followed up since our laboratory was mostly used as a primary screening center and the patients with positive IgM results were referred to the obstetrics and gynecology outpatient clinics.

CONCLUSION

In conclusion, the seroprevalence of Toxoplasma, CMV and Rubella was determined in pregnant women in our region in the two-year period between 01.01.2018 and 31.12.2019 with this study. Although these seroprevalence rates in Erzurum are generally compatible with other studies conducted in our country, Toxoplasma IgM and rubella IgG seropositivity rates were found to be lower compared to the overall incidence of our country. It will be beneficial to provide training on the routes of transmission of this disease and ways to prevent disease for expectant mothers in the regions where the prevalence of toxoplasmosis is high, and to make expectant mothers immune by investigating rubella serology in women of childbearing age in the countries under the threat of immigration.

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Ethical approval: This study was approved by the Clinical Research Ethics Committee of Ataturk University, Faculty of Medicine (2019/20).

REFERENCES

1. Inci A, Yener C, Guven D. The Investigation of toxoplasma, rubella and cytomegalovirus seroprevalencies in pregnant women in a state hospital. Pam Med J 2014;25:143-6.
2. Toklu GD. Antibodies frequency against Toxoplasmosis, Rubella Virus and Cytomegalovirus in pregnant women. J Clin Anal Med 2013;4:38-40.
3. Duran B, Toktamis A, Erden O, et al. A Contraversial issue in antenatal care: TORCH screening. Cumhuriyet Med J 2002;24:185-90.
4. Altunal LN. Seroprevalence of Toxoplasma gondii, Rubella and Cytomegalovirus among pregnant refugees and Turkish women: a retrospective comparative study. South Clin Ist Euras 2018;29:235-39.
5. Madendag Y, Eraslan Sahin M, Col Madendag I, et al. Investigation of toxoplasma, cytomegalovirus and rubella seroprevalence in pregnant women admitted to our hospital. Perinatal J 2018;26:7-10.

6. Sirin MC, Agus N, Yilmaz N, et al. Seroprevalence of *Toxoplasma gondii*, Rubella virus and Cytomegalovirus among pregnant women and the importance of avidity assays. *Saudi Med J* 2017;38:727-32.
7. Cicek AC, Duygu F, Inakci IH, et al. Investigation of *Toxoplasma gondii* antibodies with ELISA among women of childbearing age in Sanliurfa province: A three years evaluation. *J Clin Exp Invest* 2012;3:61-5.
8. Bakacak M, Bostanci MS, Kostu B, et al. Seroprevalence of *Toxoplasma gondii*, Rubella and Cytomegalovirus among pregnant women. *Dicle Med J* 2014;41:326-31.
9. Obut M, Doğan Y, Bademkiran MH, et al. *Toxoplasma*, Rubella and Cytomegalovirus seroprevalence in pregnant women in Diyarbakir. *Dicle Med J* 2019;46:23-8.
10. Mumcuoglu I, Toyran A, Cetin F, et al. Evaluation of the toxoplasmosis seroprevalence in pregnant women and creating a diagnostic algorithm. *Mikrobiyol Bul* 2014;48:283-91.
11. Tanrıverdi EC, Kadioglu BG, Alay H, et al. Retrospective Evaluation of Anti-*Toxoplasma gondii* Antibody Among First Trimester Pregnant Women Admitted to Nenehatun Maternity Hospital between 2013-2017 in Erzurum. *Turkiye Parazitoloj Derg* 2018;42:101-5.
12. Ahmadpour GR, Ezatpour B, Hadighi R, et al. Seroepidemiology of *Toxoplasma gondii* infection in pregnant women in west Iran: determined by ELISA and PCR analysis. *J Parasit Dis* 2017;41:237-42.
13. El Deeb HK, Salah-Eldin H, Khodeer S, et al. Prevalence of *Toxoplasma gondii* infection in antenatal population in Menoufia governorate, Egypt. *Acta Trop* 2012;124:185-91.
14. Sahu SK, Pradhan SK, Nayak LM. Seroprevalence of TORCH infection among pregnant women. *Int J Community Med Public Health* 2019;6:2189-94.
15. Alghamdi J, Elamin MH, Alhabib S. Prevalence and genotyping of *Toxoplasma gondii* among Saudi pregnant women in Saudi Arabia. *Saudi Pharm J* 2016;24:645-51.
16. Tekin A, Deveci O, Yula E. The seroprevalence of antibodies against *Toxoplasma gondii* and Rubella virus among childbearing age women in Mardin province. *J Clin Exp Invest* 2010;1:81-5.
17. Inci M, Yagmur G, Aksebzeci T, et al. The investigation of *Toxoplasma gondii* seropositivity in women in the Kayseri province. *Turkiye Parazitoloj Derg* 2009;33:191-4.
18. Zhang S, Hu L, Chen J, et al. Cytomegalovirus seroprevalence in pregnant women and association with adverse pregnancy/neonatal outcomes in Jiangsu Province, China. *PLoS One* 2014;9:e107645.
19. Sharma S, Duggal N, Agarwal S, et al. Seroprevalence of *Toxoplasma*, Rubella and CMV infections in antenatal women in a tertiary care hospital in North India. *J Commun Dis* 2015;47:23-6.
20. De Paschale M, Agrappi C, Manco MT, et al. Incidence and risk of cytomegalovirus infection during pregnancy in an urban area of Northern Italy. *Infect Dis Obstet Gynecol* 2009;2009:206505.
21. Kan O, Kocak O. Cytomegalovirus (CMV) screening results in pregnant women admitted to a tertiary center in the middle Anatolia. *Turk Hij Den Biyol Derg* 2019;76:423-30.
22. Enders G, Daiminger A, Lindemann L, et al. Cytomegalovirus (CMV) seroprevalence in pregnant women, bone marrow donors and adolescents in Germany, 1996-2010. *Med Microbiol Immunol* 2012;201:303-9.
23. Pembrey L, Raynor P, Griffiths P, et al. Seroprevalence of cytomegalovirus, Epstein Barr virus and varicella zoster virus among pregnant women in Bradford: a cohort study. *PLoS One* 2013;8:e81881.
24. Alvarado-Esquivel C, Terrones-Saldivar MDC, Hernandez-Tinoco J, et al. Seroepidemiology of Cytomegalovirus infection in pregnant women in the Central Mexican City of Aguascalientes. *J Clin Med Res* 2018;10:337-44.
25. Pradhan SV. Epidemiological and serological profiles of TORCH infection in pregnancy. *J Pathology Nepal* 2015;5:705-8.
26. Dempsey AF, Pangborn HM, Prosser LA. Cost-effectiveness of routine vaccination of adolescent females against cytomegalovirus. *Vaccine* 2012;30:4060-6.
27. Gurlek B, Colak S. Antenatal *Toxoplasma gondii*, Rubella and Cytomegalovirus infection screening among pregnant women attending Tertiary University Hospital. *Gynecol Obstet Reprod Med* 2019;25:74-80.
28. Roomande N, Saremi A, Pooladi A, et al. Seroepidemiological study of *Toxoplasma*, Rubella, Cytomegalovirus and Varicella zoster in women; case study of Sarem Women's Hospital. *Sarem J Reprod Med* 2019;3:65-9.
29. Muliylil DE, Singh P, Jois SK, et al. Seroprevalence of rubella among pregnant women in India, 2017. *Vaccine* 2018;36:7909-12.
30. Taku NA, Ndze VN, Abernathy E, et al. Seroprevalence of rubella virus antibodies among pregnant women in the Center and South-West regions of Cameroon. *PLoS One* 2019;14:e0225594.
31. Alvarado-Esquivel C, Hernandez-Tinoco J, Sanchez-Anguiano LF, et al. Rubella immune status in pregnant women in a Northern Mexican City. *J Clin Med Res* 2016;8:656-61.
32. Republic of Turkey Ministry of Health General Directorate of Primary Health Care Services. Extended immunization program circular. 2006 /Circular No: 120.