Original Research Article

Tetanus Immunization among Pregnant Women: Coverage rate and Rate of Protection at Time of Delivery

Abstract

Even though attempts have been effectively applied to eradicate the neonatal tetanus through widespread childhood vaccination and improved conditions at delivery, it remains major cause of infant mortality and continues a problem of public health in developing countries including Yemen. The aims of this study were to determine the tetanus immunization status, the association between the risk factors and failure of protection in pregnant women at time of delivery. This cross-sectional study included 476 women seeking care for delivery at Al Thawra Modern General Hospital and Al Sabain Hospital, women age ranged from 16-49 years old. Immunization information and factors effecting it were obtained through a standard questionnaire. Serum samples were collected and level of IgG antibody against *Clostridium tetani* was measured by ELISA technique. Protected women were defined as those with serum antibody levels > or = 0.6 IU/ml. The total vaccine covering rate of tetanus was 87%, and maternal vaccine rate was 33.6%, the protective rate at time of delivery was 68.5%. There were significant association between unvaccinated (OR=18.6), older ages (OR=1.7), rural residency (OR=34) and malaria infection during pregnancy (OR=2.9); with protection failure in pregnant women at time of delivery. It can be concluded that the total vaccine coverage rate and antenatal tetanus vaccine rate were insufficient. In addition, the protective rate at time of delivery was low and large numbers of neonate are susceptible to neonatal tetanus and death. Vaccinating every pregnant woman with at least one dose of TT would be an affordable and effective way to protect against neonatal tetanus, and would be a step toward eliminating the deaths that continue to occur due to this preventable disease in Yemen.

Keywords: Neonatal Tetanus, Coverage rate, protective rate, Tetanus vaccine, pregnancy, Sana'a city-Yemen.

Introduction

Tetanus is an acute infection, non-communicable disease with a high case fatality rate, caused by *Clostridium tetani (C. tetani)*[1]. Tetanus is a disease resulting from a specific toxin produced at site of injury by the anaerobic, spore forming organism *C. tetani* which is finding in soil and feces. Tetanus has been a major cause of death worldwide, largely due to inadequate vaccination and poor wound prophylaxis[2]. During sporulation the vegetative form of the organism develops into a spore form, giving a characteristic drumsticks appearance in blood smear. The spores of this organism are very resistant to disinfectants. Also, the spore form can survive for many years in soil [3,4]. Tetanus can affect all age groups but umbilical card infection during delivery is the most common form affecting newborn babies and mothers, case mortality of tetanus can be 100% if untreated and can range between 10-60% even under hospitalized care. There is no natural immunity against tetanus [5]. A significant number of women die every year due to maternal tetanus, most of these deaths occur in Africa, East and southern Asia [1]. The global incidence of tetanus has been estimated at approximately one million cases annually[6]. The World Health Organization[5] reported that globally 49.000 newborns died of this disease in 2013 alone. Tetanus kills one newborn every eleven minute, approximately 134 babies every day[1]. Eradication of tetanus is difficult due to the abundance of tetanus bacterial spores in the environment; the goal is to work towards elimination of tetanus through vaccination [7]. Neonatal tetanus is a

significant health problem in Yemen. Newborns can be successfully protected against tetanus by vaccinating women with tetanus toxoid, the coverage rate of vaccination with this vaccine proved to be affected by knowledge, attitude and practice of women about antenatal tetanus toxoid vaccine [8]. The World Health Organization aimed to achieve worldwide neonatal tetanus elimination by 2005, which was defined as the reduction of neonatal tetanus cases to less than 1 case per 1,000 live births in every district of every country [9,10]. However, high prevalence remained present in 21 countries including Yemen[11]. There is no recent study in Yemen that determines the vaccine coverage rate and the antibody level of tetanus at time of delivery. So, this study aimed to determine; vaccine coverage rate and the immunological status of tetanus among pregnant women at the time of delivery and factors associated of protection failure against tetanus.

Subjects and Methods

This cross-sectional study was carried out during a period of 12 months, starting in August 2017 and ending in August 2018. included 476 women seeking care for delivery at Al Thawra Modern General Hospital and Al Sabain Hospital, Sana'a city- Yemen. The study included women at time of delivery, and excluded pregnant women before time of delivery and pregnant women who are not sure about history of taking the tetanus vaccine. Serum samples were collected and measured for the level of IgG antibody against *Clostridium tetani* toxoid by commercially available ELISA technique (Roche). Protected women were defined as those with serum antibody levels > or = 0.6 IU/ml. A full history was taken from each studied individual; and the findings were recorded in a predesigned questionnaire in which data collection was based on face to face interviews.. The data collected included demographic data, number of deliveries, number of abortions, body weight, mother's knowledge about tetanus, and history of mother's tetanus vaccine and factors that might effect on immune response of women at time of delivery.

Statistical Analysis

To relate possible risk factors of vaccine failure for tetanus, the data were examined in a case-control study format. For women with evidence of vaccine failure (serum antibody levels < 0.6 IU/ml) were matched up with those who were Protected (serum antibody levels > or = 0.6 IU/ml).

Ethical Consideration

Ethical clearance for the study was taken from the Faculty of Medicine and Health Sciences Research Review Committee. Informed Consent was taken from the volunteers before the collecting specimens.

RESULTS

Table 1 shows the IgG antibody levels and the rates of protection and non-protection against tetanus among studied pregnant women at time of delivery. the protective rate at time of delivery was 68.5%, while 31.5% were not protected. Table 2 shows the association between age groups and non-protection rate against tetanus among studied pregnant women. There were significant association between older age and failure of protection in which the rate of failure in the older age group 36-49 years was 41.3% with odds ratio (OR) equal to 1.9, 95% CI= 1.1-3.2, χ^2= 6.4, p=0.01, while the rate of failure was lower in other younger age groups. Table 3 shows vaccine coverage rates and factors associated with protection failure against tetanus among pregnant women at time of delivery. The total vaccine covering rate of tetanus was 87%, and maternal vaccine rate (antenatal tetanus vaccine) was 33.6%,

also the childhood vaccine coverage was very low (0.3%), and school-age coverage rate was 40.9%. When factors of non-protection were considered, there were significant association between history of un-vaccinated women and non-protection against neonatal tetanus (NT) with protection failure rate equal to 85% and OR equal to 18.6, 95% CI= 8 -39, χ^2= 93, <0.001, rural residency with failure rate equal to 59% and OR equal to 34, 95% CI= 1.8 -6.5, χ^2= 16.2, <0.001; and malaria infection during pregnancy with failure rate equal to 59% and OR equal to 34, 95% CI= 1.8 -6.5, χ^2= 16.2, <0.001.

Discussion

Fetuses have acquired passive immunity against tetanus if their mothers are adequately immunized, two or more doses of tetanus toxoid vaccine to the mother have been shown to reduce NT mortality by 94% [12]. The WHO recommends a primary series of three doses of DTP vaccine in the first year of life and three booster doses of tetanus toxoid in later childhood, and adulthood to prevent tetanus in all ages. The target date for global maternal neonatal tetanus elimination (MNTE) was 2015. But in August 2015, elimination had not been achieved in 21 countries including Yemen [11]. This study indicated that the rate of overly protection with IgG antibody level (≥0.6 IU/ml) was 68.5% among the studied pregnant women at time of delivery in Sana'a city, Yemen. This result is similar to that reported in Turkey where the rate of protective pregnant women was 69.0% with serum antibody level (≥0.6 IU/ml) [13]. In contrast, the present result is in disagreement with previous studies where the protection rates were as follow: in Yemen (87.70%) [14], in Iraq (90%) [15] and in India (94%) [16]. This low rate in our study could be due to that most mothers received only 1 and/or 2 doses of tetanus vaccine which leaded to failure protection of mothers to produce an adequate immune response at time of delivery. Also booster doses of TT are not routinely given in Yemeni family medical practice except in cases of serious injury. In this study, there statistical significant association between the failure of protection and older age group (p >0.05).The same results were found in Iraq (p<0.05)[15], in Combodia (p<0.001) [11], and in Taiwan where the level of anti-tetanus antibodies were decline with age from 4.8IU/ml in those aged 16-19 and to 0.82-0.87 IU/ml in those aged >51years (p=0.001)[11]. However, this study was in disagreement with other studies conducted in Turkey (p>0.05) [13] and in Indonesia (p>0.05) [17] in which no effect of age in the rate of protection failure. The present study indicated statistical significant association between residence in rural areas and failure of protection among studied pregnant women (p<0.001), which disagreed with previous studies as follows: in Yemen (p=0.96) [14], in Turkey (p>0.05) [13], in Cambodia (p=0.88) [11] and in Senegal (p=0.067) [18] in which no difference in the rate of failure between rural and urban areas. This indicated that the vaccine program covered urban more than rural areas in Yemen. In the current study the total vaccine covering rate of tetanus was 87%, and maternal vaccine rate (antenatal tetanus vaccine) was 33.6%, only also the childhood vaccine coverage was very low (0.3%), and school-age coverage rate was 40.9%. which disagreed with previous studies in Turkey [13], in Cambodia [11] and in Senegal[18] in which vaccine covering rate of tetanus, maternal vaccine rate, childhood vaccine coverage rate and school-age coverage rate were above 90%. Our low rates could be due to the lack of vaccine register data base and therefore the vaccination history obtained verbally from the women may be unreliable. Also, it could be due to of the incorrect idea about vaccine contraindication with pregnancy as some women believe that taking the vaccine during pregnancy could cause abortion.

The current study found a significant association between un-vaccination with failure of protection in which the protection failure rate was 85% with OR=18.6 (p<0.001). This result is similar to previous studies conducted in India (p<0.05) [16] and in Vietnam (p<0.05) [19]. However, this result is in

disagreement with a study conducted in Portugal where the difference in antibody concentration (for both pre and post-vaccination) between those two groups were not statistically significant[20].This difference may be due to the global status of serological immunity against tetanus varies between countries as a result of different national vaccination policies and the criteria used for determination of serum levels of tetanus antitoxin. The present study, found signification association between lower rate of protection failure and taking the vaccine during pregnancy (p<0.001). This result is in agreement with a previous study which indicated that when women take the vaccine during pregnancy this would provide the highest concentration of maternal antibodies to be transferred to their fetuses[21]. In this study, a statistical significant association between taking the last dose of tetanus vaccine and low failure rate of protection was found (14.8%) p=0.041). This result agreed with previous studies in other countries where the failure protection rates were as follow: in Iraq (8%), [15], and in Tanzania (5.1%) [22]. The current study found statistical significant association between the malaria infection and failure of protection (57%, p<0.001). This result is in agreement with studies reported in Gambia [23], and in Kenya[24]. This result can be explained by the findings of Cumberland *et al*[25] in which mother infected with malaria had reduce level of antibodies in spite of vaccination also they found that placental malaria reduce transfer of antibody to fetus [25]. This result reflects the negative effect of malaria in immune system particularly in humeral immunity.

Conclusion

In conclusion, the total vaccine covering rate and antenatal tetanus vaccine rate were insufficient. In addition, the protective rate at time of delivery was low and large numbers of neonate are susceptible to neonatal tetanus and death. Vaccinating every pregnant woman with at least one dose of TT would be an affordable and effective way to protect against neonatal tetanus, and would be a step toward eliminating the deaths that continue to occur due to this preventable disease in Yemen.

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Conflict of interest:

"No conflict of interest associated with this work".

Author's contribution

This research work is part of a MSc. thesis. The candidate is the first authorr (ZAHSA) who conducted the laboratory and field works; and wrote up the thesis. The corresponding author (HAA) and (AYA) supervised the laboratory and field works, revised and edited the thesis draft and the manuscript and AAS helped in conducted the clinical work.

References

1-Alex-Hart B A and Okoh BAN. Awareness and Status of Tetanus Toxoid Vaccination among Female Undergraduate Students in a Nigerian University. International J Tropical Disease and Health 2015; 7(1):6-5.

2-Skuby SO, Rhee E, Thilo EH *et al.* Tetanus and Occam's Razor: Almost Forgotten but Not Gone: A Case Report. Pediatrics 2016; 138(5):1- 5.

3-Radostits O M, Gay CC, Hinchcliff K W *et al.* Veterinary Medicine E-Book: A textbook of the diseases of cattle, horses, sheep, pigs and goats. Elsevier Health Sciences 2007.

4-Khan A, Raza SHA, Saeed M. *et al.* Diagnosis and Therapeutic Management of Tetanus in Female Buffalo Calf at Tandojam, Sindh, Pakistan. World 2016; 6 (2):66-69.

5-World Health Organization. Elimination of Maternal and Neonatal Tetanus [http://www.unicef .Org / supply/ 2015; index 5214 html.

6-Hassel B. Tetanus: pathophysiology, treatment, and the possibility of using botulinum toxin against tetanus-induced rigidity and spasms. Toxins 2013; 5(1):73-83.

7-Rodrigo C, Fernando D and Rajapakse S. Pharmacological management of tetanus: an evidence-based review. Critical Care 2014; 18 (2):217.

8-Dhia T and Baiee HA. Knowledge and Practice of Mothers about Antenatal Tetanus Toxoid Vaccination in AL-Hilla City. J of Babylon university / pure and applied sciences 2017; 3 (25):1098-1104.

9-Chang SC and Wang CL. Neonatal tetanus after home delivery: report of one case . Pediatrics and Neonatology 2010; (51(3):182-185.

10- World Health Organization. Tetanus Vaccines: WHO position paper – February 2017 weekly Epidanolohical Record 2017; 6 (92):53-76.

11-Scobie H M, Mao B, Buth S *et al.* Tetanus immunity among women aged 15 to 39 years in Cambodia: a national population-based sero-survey, 2012. Clinical and Vaccine Immunology 2016; 23 (7):546-554.

12-Ibinda F, Bauni E, Kariuki SM *et al.* Incidence and risk factors for neonatal tetanus in admissions to Kilifi County Hospital, Kenya. *Plos One* 2015; 10(4):1-3.

13-Maral I, Cirak M, Aksakal F N *et al.* Tetanus immunization in pregnant women. Serum levels of ant tetanus antibodies at time of delivery. European J of epidemiology 2001; 17(7):661-665.

14-Mojalli,S.M., AL Madhagi, A., AL Shamahy., AL Hadad, A. Tetanus immunization status and factors affecting the vaccine among women of childbearing age in Sana'a city Yemen. MSC thesis Faculty of the Medicine and Health Sciences Sana'a Yemen 2011.

15-Hurmez L, Habeeb Q S, and Al Derzi N A. Seroprevalence of tetanus antibodies among pregnant women in Duhok Governorate, Iraq. East Mediter health J 2012; 18 (6): 8-573.

16-Subodh B, Vijay G, Amita G *et al.* Safety and immunogenicity of tetanus toxoid in pregnant women. J Obstet Gynecol India 2009; 3 (59):224-227.

17-Roosihermiatie B, Nishiyama M, and Nakae K. Factors associated with TT (tetanus toxoid) immunization among pregnant women, in Saparua, Maluku, Indonesia. Southeast Asian J Trop Med Puplic Health 2000; 31 (1):91- 95.

18-Leroy O and Garenne M. Risk factors of neonatal tetanus in Senegal. International J of epidemiology 1991; 20 (2):521-526.

19-Sangpetchsong V A, Vichaikummart S A, Vichitnant A A *et al.* Transfer rate of transplacental immunity to tetanus from non-immunized and immunized mothers. The Southeast Asian J of tropical medicine and public health 1984; 15(3):275-280.

20-Gonçalves G, Santos M A, Frade J G *et al.* Levels of diphtheria and tetanus specific IgG of Portuguese adult women, before and after vaccination with adult type Td. Duration of immunity following vaccination. BMC Public health 2007; 7(1):109.

21-Healy G M, Rench MA, Baker G J. Importance of timing of maternal Tdap immunization and protection of young infants. Clin infect Dis 2013; 56:539-44.

22-Aboud S, Lyamuya E F, Kristoffersen E K *et al.* Tetanus immunity among pregnant women attending antenatal care in Dar es Salaam, Tanzania. African J of reproductive health 2002; 6(2):87–93.

23-Okoko B J, Wesumperuma L H, Pinder M. *et al.* . The influence of placental malaria infection and maternal hyper-gamma-globulinemia on transplacental transfer of antibodies and IgG subclasses in a rural West African population . The J of infectious diseases 2001; 184 (5):627-632.

24-Brabin B J, Nagel J, Hagenaars A M *et al.* The influence of malaria and gestation on the immune response to one and two doses of adsorbed tetanus toxoid in pregnancy. Bulletin of the World Health Organization 1984; 62(6):919.

25-Cumberland P, Shulman C E, Chris Maple P A *et al.* Maternal HIV infection and placental malaria reduce transplacental antibody transfer and tetanus antibody levels in newborns in Kenya. The J of infectious diseases 2007; 196 (4):550-557.

Table 1: The IgG antibody levels and the rates of protection and non-protection against tetanus among studied pregnant women at time of delivery in Sana'a city, 2018

IgG Antibody Levels in IU/ ml	**No.**	**%**	***P***	**Interpretation**
< 0.6 IU/ml	150	31.5	<0.05	Susceptible for neonatal tetanus
≥ 0.6 IU/ml	326	68.5		Protective for neonatal tetanus
total	476	100		

Table 2: The association between age groups and non-protection against tetanus among studied pregnant women in Sana'a city, 2018

Age groups/years	**No protection n=150**		**OR**	**CI**	χ^2	***P***
	No.	%				
16-25 n=234	72	30.7	0.88	0.0-1.3	0.39	0.53
26-35 n=167	45	26.9	0.71	0.4 -1.08	2.4	0.11
36-49 n=75	33	44	1.9	1.1-3.2	6.4	0.011
Total=476	150	31.5				

OR Odds ratio >1 (**at risk**)
CI Confidence intervals 95%
χ^2 Chi-square 03.9 (**significant)**
p Probability value <0.05 (**significant**)

Table 3: Vaccine coverage and factors associated with protection failure against tetanus among pregnant women at time of delivery, in Sana'a city, 2018

factors	Vaccine coverage	No protection n=150 No.	%	OR	CI	χ^2	*P*
Vaccination							
Infancy (3DPT) n= 373	373/476 78.4%	76	20.4	0.04	0.02-0.07	151	<0.001
Childhood 1 dose n=30	30/476 6.3%	4	13.3	0.3	0.1-0.89	5.1	0.02
School age 1 dose N=195	195/476 40.9%	35	17.9	0.2	0.19-0.46	30.8	<0.001
Vaccination during pregnancy							
2 doses (27 and 36 gestation) n=160	160/476 33.6%	19	11.9	0.18	0.1-0.3	45	<0.001
One dose n=27	27/476 5.7%	4	14.8	0.3	0.1-1	3.9	0.047
*MALARIA n=14	14/14 100%	8	57.1	2.9	1.0-8.5	4.1	0.041
Total vaccinated n=414	414/476 87%	97	23.4	0.0	undefined	126	<0.001
Total unvaccinated n=62	62/476 13%	53	85	18.6	8.8-39	93	<0.001
Residency							
Urban n=432	392/432 90.7%	124	28.7	0.13	0.06-0.3	30	<0.001
Rural n=44	22/44 50%	26	59	34	1.8-6.5	16.2	<0.001

*All vaccinated at 27 and 36 gestation dose

OR Odds ratio >1 (**at risk**)
CI Confidence intervals 95%
χ^2 Chi-square 03.9 (**significant*)***
p Probability value <0.05 (**significant**)