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Review

Neonatal tetanus elimination in Pakistan: progress and challenges

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SUMMARY

Pakistan is one of the 34 countries that have not achieved the neonatal tetanus (NT) global elimination target set by the World Health Organization (WHO). NT, caused by *Clostridium tetani*, is a highly fatal infection of the neonatal period. It is one of the most underreported diseases and remains a major but preventable cause of neonatal and infant mortality in many developing countries. In 1989, the World Health Assembly called for the elimination of NT by 1995, and since then considerable progress has been made using the following strategies: clean delivery practices, routine tetanus toxoid (TT) immunization of pregnant women, and immunization of all women of childbearing age with three doses of TT vaccine in high-risk areas during supplementary immunization campaigns. This review presents the activities, progress, and challenges in achieving NT elimination in Pakistan.

A review of the literature found TT vaccination coverage in Pakistan ranged from 60% to 74% over the last decade. Low vaccination coverage, the main driver for NT in Pakistan, is due to many factors, including demand failure for TT vaccine resulting from inadequate knowledge of TT vaccine among reproductive age females and inadequate information about the benefits of TT provided by health care workers and the media. Other factors linked to low vaccination coverage include residing in rural areas, lack of formal education, poor knowledge about place and time to get vaccinated, and lack of awareness about the importance of vaccination. A disparity exists in TT vaccination coverage and antenatal care between urban and rural areas due to access and utilization of health care services. NT reporting is incomplete, as cases from the private sector and rural areas are underreported. To successfully eliminate NT, women of reproductive age must be made aware of the benefits of TT vaccine, not only to themselves, but also to their families. Effective communication strategies for TT vaccine delivery and health education focusing on increasing awareness of NT are strongly suggested. It is imperative that the private and government sectors work cooperatively to report NT cases and improve routine TT vaccination coverage.

1. Introduction

Neonatal tetanus (NT), a highly fatal infection of the neonatal period, is caused by the bacterium *Clostridium tetani*. NT develops when the umbilical cord becomes contaminated with *C. tetani* spores as a result of unhygienic delivery or cord care practices after delivery.[1,2] The disease usually occurs in rural settings with poor access to health facilities.[3,4] Surveillance systems do not capture those NT deaths that occur at home and those for whom medical care at a hospital was not sought, with birth and death not being reported.[3,4] NT is one of the most underreported diseases[5] and remains a major but preventable cause of infant and neonatal mortality in many developing countries.[6,7]

In 1989, the World Health Assembly called for the elimination of NT by 1995; by the year 2000, 104 of 161 developing countries had achieved elimination.[8] As of February 2012, Pakistan is one of the 34 countries that have not achieved maternal and neonatal tetanus (MNT) elimination.[9] The MNT Elimination Initiative, the global initiative launched by the United Nations Children's Fund (UNICEF), World Health Organization (WHO), and the United Nations Population Fund (UNFPA), continues to spearhead the effort to eliminate MNT beyond 2005, the target date for worldwide elimination of the disease.[10] However, progress in global elimination has been delayed due to slow implementation of the recommended strategies.[3,9]

To achieve NT elimination, the WHO recommends that countries conduct surveillance for cases of NT in high-risk areas, in addition to promoting clean delivery services, routine immunization of pregnant women, and the 'high-risk approach' of targeting women of childbearing age living in high-risk areas with three doses of tetanus toxoid vaccine (TT or Td), implemented

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as 'supplemental immunization activities' (SIAs).[3] The WHO defines global elimination as an annual rate of <1 case of NT per 1000 live-births at the district level; maternal tetanus is considered eliminated when NT is eliminated.[10]

NT remains a public health problem in Pakistan where it is estimated that the current reporting system captures less than 10% of cases.[11–14] In 1988, 10 countries including Pakistan accounted for more than 70% of all NT deaths worldwide and were targeted for focused activities.[15] The estimated global number of NT deaths was 248 000 in 1997, and 26 400 of these deaths were in Pakistan, with an NT mortality rate of 5 per 1000 live-births.[16] By the year 2008, the WHO estimated that the global NT mortality had declined to 59 000,[17,18] a 92% reduction from the situation in the late 1980s.[17] NT has been actively integrated into the acute flaccid paralysis (AFP)/polio surveillance infrastructure in Pakistan; it is hoped that this integration will improve the reporting efficiency of NT and enhance effective monitoring of TT vaccination coverage.[19] Nevertheless, underreporting of NT remains a public health concern for global elimination and hinders effective surveillance.[19,20]

The Government of Pakistan has set the target to eliminate MNT by 2015.[21] The Government is committed to the goal of reducing the incidence of MNT to <1 case per 1000 live-births in all districts of the country. To achieve this, the Pakistan National Plan for Immunization has adopted the 'high-risk approach'.[14] Pakistan has made good progress in the last 10 years since the high-risk approach strategy was initiated. By the end of 2010, at least three rounds of SIAs had been implemented in 54 out of a total of 135 districts, compared to 64 out of a total of 121 districts in Pakistan by the end of 2003.[22] Coverage with the third dose of TT vaccine was 84% during the first phase and 73% during the second phase of the SIAs conducted between 2001 and 2003.[22] This review presents the activities, progress, and challenges in achieving NT elimination in Pakistan.

2. Methods

2.1. Literature search

We systematically reviewed the published and gray literature to assess the NT elimination activities in Pakistan. Medline, PubMed, EMBASE, Global Health, and Cochrane databases were searched in January 2012, as were the reference lists of relevant publications. We used the following combinations of search terms: (Tetanus OR Tetanus Toxoid OR Clostridium tetani OR tetanus antibod*) AND (Pakistan*) AND (neonat* OR infan* OR newborn*). In addition, we searched and extracted information on immunization coverage from a variety of sources, including the official WHO reported immunization data, UNICEF, Pakistan Demographic and Health Surveys, Pakistan Social and Living Standards Measurement Surveys, and other studies from the government and private sectors.

2.2. Selection of studies

Studies were included if they focused on the 'population' of neonates and on tetanus in Pakistan. We considered both randomized trials and observational studies meeting these criteria. We excluded non-English publications.

2.3. Data extraction

Relevant data were extracted from the identified studies by two independent researchers (JL and TN), who also performed quality assessment using a tool adapted from STROBE (Strengthening the Reporting of Observational Studies in Epidemiology).[23] Information extracted included the location of the study, study design, sample size, outcome measure, and main results. Results of the quality assessments were compared and differences discussed until consensus was reached.

3. Descriptive epidemiology of neonatal tetanus

NT is a highly fatal infection of the neonatal period. *C. tetani*, the causative organism, is a ubiquitous bacterium in soil and the contents of animal and human intestines.[2] Contamination of the umbilical cord may occur through cutting the cord using an unclean instrument or applying substances containing tetanus spores to the stump.[24] If contamination occurs when the cord is cut or within the next few days, symptoms begin 3–12 days after birth.[3,25] Tetanus toxin (tetanospasmin), a potent neurotoxin produced by the vegetative forms of *C. tetani*, causes increased irritability of the central nervous system and exaggerated motor activity by blocking inhibitory neurotransmitters,[24] resulting in muscular stiffness and spasms.[24,26]

The geographical location of a given country and its climate influence the incidence of tetanus.[27] The disease often has a focal distribution, consistently occurring in clusters in geographical areas and population groups with poor birth hygiene[28] and where shared behaviors or the environment enhance the risk of cord contamination.[13] It commonly occurs in densely populated areas and hot, humid climates with soil rich in organic matter which creates favorable conditions for the maintenance of *C. tetani*.[27]

NT shows a seasonal pattern with a higher incidence of NT cases and deaths occurring in the rainy season (July to November peak) than during the dry season (Figure 1). The rise in monthly case reports and deaths begins with the onset of the monsoon, usually in July, peaks between August and October, and falls in November. This pattern has been observed in India and Pakistan.[29–31] There is speculation that the seasonal increase in NT may be related to an increased risk of contamination of the cord stump with tetanus spores in the environment, which becomes increasingly overcrowded during July to October.[30]

NT is more prevalent in rural settings with poor access to health facilities.[32] The incidence of tetanus has been found to be 5- to 12-times higher in rural areas.[13,15] In Dadu District, Pakistan, the risk of NT was found to be 8-times greater in rural than in urban areas.[33] However, urbanization and the rapid expansion of cities in Pakistan have made urban areas increasingly vulnerable to NT.[27,34] Urban areas often have lower NT incidences compared to rural areas due to better access to care and better hygiene conditions.[34,35]

Factors influencing NT mortality rates are age of onset of symptoms, birth weight, age on admission, age at death, sex distribution, conditions of antenatal care and delivery, and TT

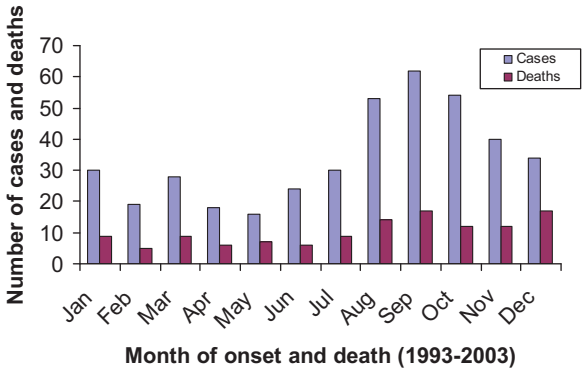

Figure 1. Distribution of neonatal tetanus cases by month of onset and death, Dadu District, Pakistan, 1993–2003.

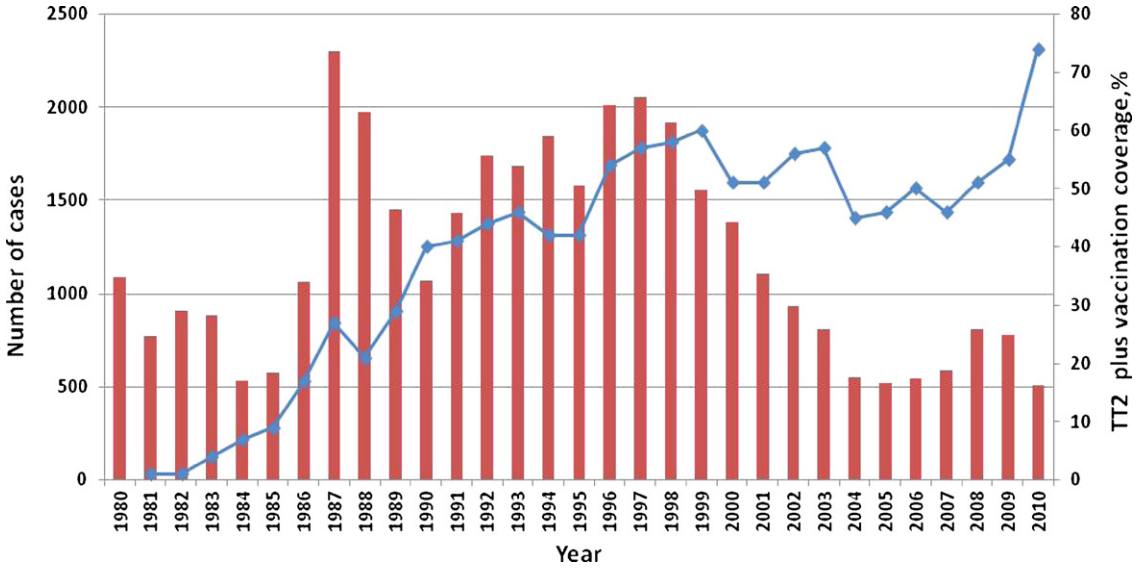

Figure 2. Neonatal tetanus annual reported cases and TT2 plus (two or more doses of tetanus toxoid vaccine) coverage, Pakistan 1980–2010 (source World Health Organization[43–45]).

immunization of women of childbearing age.[12] Community-based mortality surveys in Pakistan have shown that the mean age of onset for NT varies from 5.5 to 7.3 days,[25,36–38] in contrast to the mean age of onset varying from 5.2[39] to 6.3 days[33] based on hospital surveillance reports. The incubation period for NT can vary from 3 to 21 days.[1] In Pakistan, an incubation period of 6 days or less and age on admission of 8 days or less were found to be significantly associated with mortality.[33] This mortality risk is exacerbated for low birth weight neonates.[40] Case fatality rates (CFR) can vary between 10% and 70% depending on treatment, age, and the health status of the infant.[26] The incubation period is related to the prognosis – the shorter it is, the greater the CFR.[40,41] Studies have shown that the CFR may be decreasing due to targeted TT immunization in Pakistan.[33,39] In a previous hospital-based surveillance report in Pakistan, the mean age at death was 10.7 days.[33]

There is a higher incidence of male than female cases.[19,20,32,33,42] This has been linked to gender bias in health care seeking practices and to cultural practices giving preference to the survival of male children.[20,33] Another cause of the higher incidence of NT among males is that male neonates are circumcised on or before the 7th day after birth depending on cultural practices in the area.[32]

Figure 2 shows the trend in annual NT reported cases and TT2 (two doses of tetanus toxoid vaccine) coverage in Pakistan from 1980 to 2010. The number of NT cases reported declined from 1085 in 1980 to 508 in 2010. Between 1990 and 1999, TT2 immunization increased 20% and then declined over the course of a decade from 60% in 1999 to 51% in 2008. In 2010, 74% of pregnant women received a protective course of TT2.[43–45]

4. Comparative studies of neonatal tetanus in Pakistan

The comparative epidemiological analysis of NT in Pakistan allowed us to evaluate the following: commonly identified risk factors for NT, their relevance to MNT elimination strategies, NT mortality levels and trends, the impact of TT immunization on NT mortality, and the role of surveillance in monitoring disease control efforts. The literature search yielded 29 original articles that allowed direct comparison because they were all carried out in different areas of Pakistan, used a similar case definition of NT for case ascertainment, and had similar control populations, if provided. Excluding case series and case reports, we identified nine case–control studies,[7,25,34,36–38,46–48] nine cross-sectional studies,[49–57] three community-based mortality surveys,[6,31,32] two quasi-randomized trials,[39,58] four descriptive studies,[19,20,33,59] one community-based randomized trial,[60] and one prospective cohort study[61] (Table 1).

4.1. Case–control and community-based studies

Table 2 shows the neonatal mortality rate, NT mortality rate, TT2 vaccination coverage levels and trends in Pakistan for studies carried out from 1981 to 2009.[6,7,25,31,32,37,38,54,61–67] The NT mortality survey carried out in the early 1980s can be used for historical comparison.[32] The results illustrate that as neonatal mortality gradually declines, the proportions of neonatal deaths due to tetanus decrease. In Pakistan, NT mortality accounted for 17% to 60% of all neonatal deaths. Community-based mortality surveys further confirmed that mortality rates were highest in areas where the risk of NT was greatest. A high degree of contact with *C. tetani* spores occurs in rural and semi-nomadic areas where people are engaged in livestock raising and live in close contact with animals. This facilitates an environment that enhances exposure to *C. tetani* spores resulting in the risk of cord contamination.[32] The contribution of NT mortality to all neonatal mortality was found to vary within and across the provinces, but was much higher in rural than urban areas (Table 2).

These high-risk areas for NT were the subject of extensive studies in Pakistan during the 1980s and 1990s. Case–control studies identified risk factors for NT by comparing children with and without NT (Table 1). Analysis of the risk factors has understandably focused on rural populations where the risk is greatest, but one study showed that there is also a risk of NT in peri-urban areas.[34] With regard to the policy implications, risk factors identified in case–control studies of NT have given rise to opportunities for preventive measures and priorities in intervention.[46]

Several studies have identified a history of NT in a mother's previous children as being a significant risk factor for NT.[36,37,46] Enhanced community-based NT reporting and surveillance may improve the identification of mothers of NT cases and mothers with a previous NT case. Following implementation of SIAs in high-risk areas, the WHO recommends enhanced case-based investigation and case-response activities mounted around each case.[68] The

Table 1
Comparative studies of neonatal tetanus in Pakistan

Place	Sample size (number of cases, number of controls)	Main findings	Ref.
Case–control studies			
NWFP	69 cases, 207 controls	Application of ghee to wound stump, PAR[a] % = 43	38
NWFP	102 cases, 306 controls	Application of ghee made in home from cow's milk (OR 1.94, 95% CI 1.07–3.53) Non-academically trained delivery attendants (OR 3.90, 95% CI 1.02–14.88)	46
Peshawar, NWFP	100 cases, 300 controls	In-use of ghee during the first few days of life (OR 1.76, 95% CI 1.02–3.1)	36
Rural parts of the northern areas of Pakistan	354 (59 cases, 295 controls)	Bundling within the first 3 days of life (OR 2.5, 95% CI 1.3–4.9); PAR% = 23	37
Rural parts of Punjab Province	211 cases, 633 controls	Interaction of pre-delivery exposure of mothers to ghee and delivery on a surface prepared with dried cow dung (OR 5.8)	25
Punjab Province	133 cases, 399 controls	The lack of topical antibiotics in circumcision wounds is a significant risk factor of NT (OR 4.2, 95% CI 1.4–12.6)	47
Rural areas of Punjab Province	229 cases, 687 controls	Ghee applications to umbilical wounds when heated with cow dung fuel was significantly associated with NT (OR 2.7, 95% CI 1.1–6.6)	48
Loralai District, Balochistan Province	41 cases, 123 controls	Risk factors were use of soil as delivery surface (OR 3.2, 95% CI 1.1–10.2) (PAR% = 64), father's illiteracy (OR 3.2; 95% CI 1.3–8.1), and possession of sheep at home (OR 2, 95% CI 1.0–5.0)	7
Karachi, Sindh Province	125 cases, 250 controls	Application of substances on umbilical cord (OR 5.1, 95% CI 2.7–9.7) (PAR% for subsequent cord application = 69), home delivery (OR 1.8, 95% CI 1.1–3.1) (PAR% = 31), and illiterate mother (OR 1.6, 95% CI 1.0–2.0)	34
Cross-sectional studies			
Peshawar, NWFP	646 females interviewed; 326 in urban, 320 in rural areas	TT2 vaccination coverage was 65% Marital status (OR 8.5, 95% CI 4.7–15.6), visits of LHW to household (OR 2.3, 95% CI 1.4–3.9), and restriction on TT vaccination (OR 28.7, 95% CI 3.5–237.9) were significantly associated with vaccination status among all females	49
Karachi, Sindh Province	60 females	TT vaccination coverage was 40.6% Inadequate knowledge about TT vaccine among reproductive age females and inadequate information about the benefits of TT provided by health care workers and media	50
Lahore District, Punjab Province	362 married females	TT2 vaccination coverage in last pregnancy was 87% Reasons for low coverage were reported as poor knowledge of place and time to get vaccinated and the importance of vaccination	51
District Bhakkar, Punjab Province	48 TBAs	12% of trained TBAs knew about cord care; no trained or untrained TBAs had sound knowledge regarding the prophylaxis of NT	52
Karachi, Sindh Province	210 women and their children	TT2 vaccination coverage for index pregnancy was 57.3% Reasons for not receiving vaccination were reported as no benefit, distant vaccination centers, pain due to vaccine, social problems and fear of harm to fetus	53
Karachi, Sindh Province	565 women	TT2 vaccination coverage was 79%; 54.5% of women had ≥4 antenatal care visits; 56% delivered at a health care facility	54
Hyderabad City, Sindh Province	307 women	TT2 vaccination coverage was 40.4% Reasons for low coverage were lack of formal education (75.2%) and lack of awareness about the importance of vaccination; LHVs and LHWs provided information about TT vaccination to 55% of women	55
Karachi, Sindh Province	1407 college/university females	83.5% of students were aware of tetanus immunization programs for females of reproductive age; 60.2% were not vaccinated at all; low immunization coverage despite good awareness of program	56
Kasur District, Punjab Province	104 married women	60% of married women sampled received ≥2 doses of TT	57
Community-based mortality surveys			
Punjab Province, Sindh Province	13 858 live births	NT mortality rates were higher in rural areas (34–42/1000 LB) compared to urban areas (18/1000 LB)	32
Balochistan, NWFP, and FATA	54 834 households	Neonatal mortality rate was 57/1000 LB; tetanus accounts for 18.3% of deaths in the neonatal period	6
Lahore, Pakistan	1476 infants	Neonatal mortality rate: 56/1000 LB; NT mortality rate: 9/1000 LB	31
Quasi-randomized trials			
Peshawar, NWFP	100 babies	Overall CFR was 48%; the case fatality for the treatment group (pyridoxine) was 23.7% as compared to 55.1% for the control group	39
Lahore, Punjab Province	100 neonates	The treatment arm had a CFR of 30% compared to the control arm with a CFR of 60%	58
Descriptive studies			
Loralai district		SIAs could prevent 280 cases of NT and 224 deaths from NT; SIAs are highly cost-effective	59
Dadu District, Sindh Province	408 neonates	The use of recapture–capture method in routine surveillance increased average annual incidence of NT from 0.55/1000 LB to 0.62/1000 LB; males had higher incidence rates than females	19
Dadu District, Sindh Province	408 neonates	Overall completeness of routine reporting was 59.2%; the proportions of cases reported were 68.1% and 53.8% for government hospitals and private reporting sites, respectively	20

Table 1 (*Continued*)

Place	Sample size (number of cases, number of controls)	Main findings	Ref.
Dadu District, Sindh Province	408 neonates	Overall NT CFR was 30%; CFR fell from 42% in 1993 to 29% in 2003; NT incidence declined from 0.90/1000 LB in 1994 to 0.18/1000 LB in 2003 A strong predictor of mortality was age at admission of 8 days or less	33
Community-based randomized trial			
Hala Districts, Sindh Province	8 village clusters (315 villages, total population 138 600)	In intervention villages, neonatal mortality rate significantly declined from 57.3 to 41.3 per 1000 LB	60
Prospective population-based cohort study			
Latifabad, Hyderabad, Pakistan	1369 pregnant women	Causes of neonatal mortality were immaturity-related, birth asphyxia or hypoxia and infections	61

CFR, case fatality rate; CI, confidence interval; FATA, Federally Administered Tribal Areas; LB, live-births; LHV, lady health visitor; LHW, lady health worker; NT, neonatal tetanus; NWFP, North West Frontier Province; OR, odds ratio; PAR, population attributable risk %; SIA, supplemental immunization activities; TBA, traditional birth attendant; TT, tetanus toxoid vaccine; TT2, two doses of tetanus toxoid vaccine.

failure of the surveillance system to detect children of mothers with histories of NT cases adds to the burden of NT mortality in the community. The population attributable risk (PAR %) for NT in a mother with a previous NT case was estimated to be between 25% and 33%.[36,38]

The PAR % for the risk factors cited in several studies, including bundling (23%),[37] soil surface as delivery surface (64%),[7] home delivery (31%),[34] and subsequent cord application (69%),[34] provide opportunities for prevention of NT and reduction in the incidence of NT through modification of health-related behaviors including birth practices.[34] Education has an important role to play, as it may motivate a change in health-related behaviors such as birth practices and consequently reduce the risk of exposure to the disease.[69] The finding that the practice of bundling was mainly linked to the first 3 days of life suggests that the risk of umbilical wound contamination may generally be confined to the first few days of life.[37] This calls for the importance of addressing post-delivery sources of NT, as others have previously suggested.[37] We present a conceptual framework for proximate risk factors and upstream determinants of NT in Figure 3.

Data from community-based NT mortality surveys and case–control studies suggest that over 90% of deliveries take place at home, assisted by relatives in 52–60% of deliveries.[7,46] Clean delivery coverage could be improved by distributing clean delivery kits to women in rural areas where delivery commonly takes place at home.[54,60] Community-based NT mortality studies showed that between 20% and 55%[37,38] of NT cases identified in the community were seen, diagnosed, and treated by a physician during their illness. However, it is difficult to speculate on the number of cases that were actually reported to the routine surveillance system, as surveillance data suggest substantial underreporting of cases.[19,20] In addition, community-based mortality studies provide some evidence for the effectiveness of maternal immunization in reducing the risks of NT (Table 2).

4.2. Cross-sectional studies

The cross-sectional surveys of TT vaccination coverage and knowledge, attitudes, and practices have shown that the main driver for NT is low maternal tetanus vaccination. These studies show that only 40.4% to 65% (Table 1) of pregnant women in Pakistan received a protective course of vaccination with two or more doses of TT (TT2+);[49,55] however surveys conducted between 2005 and 2006 showed that TT2+ coverage ranged from 60% to 65%.[49,57] First, this estimate is close to the 53.4% (Table 2) found in the 2006/2007 Pakistan Demographic and Health Survey (DHS),[62] and second, despite the underestimation of administrative coverage, the trend in annual reported TT2+ coverage seems to confirm this estimate (Figure 2). However, there was a wide discrepancy in TT coverage between and within provinces and districts in Pakistan.[51] The trend is that of increasing TT2+ coverage as confirmed by the Pakistan DHS 1990/91[62] and 2006/2007;[65] the

Table 2
Comparison of trends in neonatal mortality, NT mortality, and TT2+ vaccination coverage

Year of survey/study	Place	Neonatal mortality rate/1000 LB	NT mortality rate/1000 LB	Proportion of NT mortality %	Maternal TT2+ vaccination coverage	Ref.
1981	Punjab Province	52	31	60	0	32
1984–1987	Lahore, Punjab Province	56	9.5	17	-	31
1988	NWFP	21	13	62	7	38
1990	Rural Punjab Province	18	11.6	64	7	25
1990/1991	All provinces	56	-	-	23.3	62
1991	Rural parts of the Northern areas		11		11.1	37
1990–1994	Balochistan and NWFP including the FATA	57	10.4	18.3	-	6
1997	Balochistan Province	61	23	38	5	7
2003–2005	Hyderabad Sindh Province	47	-	-	-	61
2004/2005	All provinces				51	63
2005/2006	All provinces				62	64
2006	Karachi Sindh Province	27			88	54
2006/2007	All provinces	54			53.4	65
2006/2007	All provinces				56	66
2008/2009	All provinces				68	67

FATA, Federally Administered Tribal Areas; LB, live-births; NT, neonatal tetanus; NWFP, North West Frontier Province; TT2+, two or more doses of tetanus toxoid vaccine.

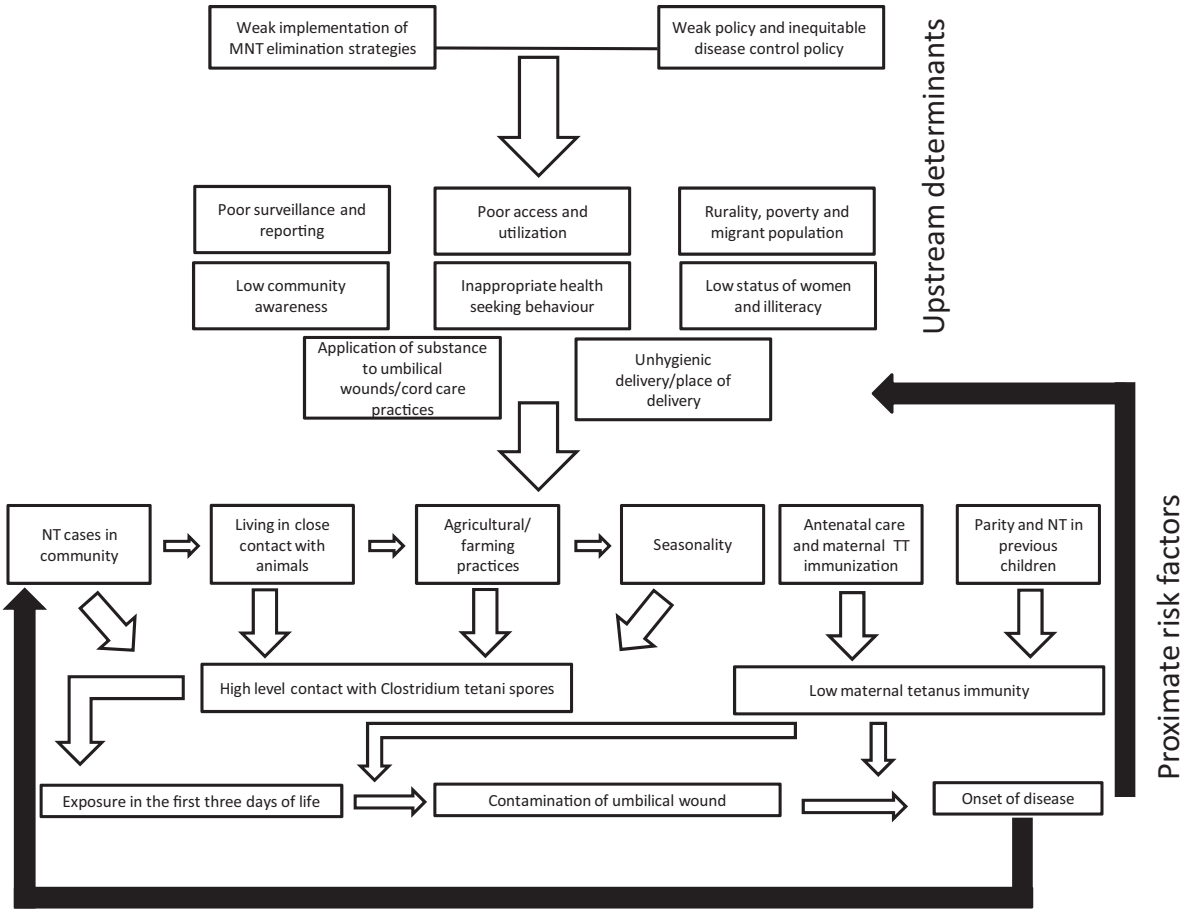

Figure 3. Framework for proximate risk factors and upstream determinants of neonatal tetanus.

highest and lowest coverage in both surveys were reported from Punjab and Balochistan provinces, respectively.

Our analysis shows that there is a demand failure for TT vaccine resulting from many factors, including but not limited to inadequate knowledge of TT vaccine among reproductive age females and inadequate information about the benefits of TT provided by health care workers and the media,[50] residing in rural areas,[49] lack of formal education,[55] and poor knowledge of place and time to get vaccinated and lack of awareness about the importance of vaccination.[51] Interestingly, knowledge about TT vaccine, antenatal visits, and visits of lady health workers (LHWs) have a significant impact on TT coverage and were found to be important factors in the increase in TT vaccination.[49] There were also disproportionate disparities in urban–rural coverage rates in TT vaccination and antenatal care; the coverage rates were higher in urban than rural areas.[49] The differences in urban–rural coverage rates, similar to those reported by the Pakistan DHS,[62–64,66,67] may be attributed to access and utilization of health care services and the health-seeking behavior of urban residents in comparison to rural residents. For example, 79% of pregnant women in urban areas compared to only 50% in rural areas sought antenatal care practices in Peshawar, Pakistan.[49] It is also common for women to have knowledge of the importance of TT vaccination provided they have access to health care services.[49] Concern has been expressed regarding the finding of low TT vaccination coverage despite good awareness of the immunization program among female students in urban areas.[56] This may have important policy implications and reflects the need to reduce the risk of NT in future cohorts of females of reproductive age by having in place school-based immunization, in combination with the diphtheria–tetanus–pertussis vaccine given in infancy.

5. Enhancing neonatal tetanus case reporting and surveillance in Pakistan

5.1. Neonatal tetanus reporting systems in Pakistan

NT is a reportable disease in Pakistan and it is reported separately from other tetanus cases.[19] Pakistan has made rapid progress towards the elimination of NT. To address the global NT elimination goal of reducing the NT incidence to <1 case/1000 live-births in every district in Pakistan, there is the need for better population-based data on the completeness of reporting of NT, incidence, and analysis to inform decision-makers who must plan and implement control measures for NT elimination.[19] However, an assessment of the completeness of ascertainment of disease reporting systems for NT is difficult for several reasons. First, most NT deaths occur at home, with birth and death not reported.[3] Second, we do not know the proportion of NT cases for whom health care is sought. And third, despite underreporting, the true number of NT cases in the community is not known.[20] Although the incidence rates reported in one study are below the global elimination goal, the surveillance data suggest substantial under-reporting, as the number of cases and NT incidence rates vary from one geographical area of a district to another.[33]

In Pakistan, two separate and parallel surveillance systems are used to monitor childhood vaccine-preventable diseases including NT: the Expanded Programme on Immunization (EPI) and the District Management Information System (DMIS) (formerly the

Hospital Management Information System). This overlap between the EPI and other reporting systems might have resulted from a lack of coordination between the EPI and DMIS teams at the district level with consequent loss of efficiency in data correlation.[70–72] However, one limitation of the NT data collected through DMIS is the lack of detailed information on clinical presentation, demographic details, and immunization status.[73] Improvement in the quality and utility of the data could also be enhanced through coordination between the DMIS and EPI at the district level. Cross-border collaboration and cross-notification of cases should be encouraged, as a substantial proportion of unreported NT cases could be found in tertiary referral hospitals in the areas adjacent to a district.[19]

5.2. Data collection, case investigation, and surveillance

Beginning 2004, NT was actively integrated into the AFP/polio surveillance infrastructure and districts began to include suspected NT and measles in the monthly reports. Data pertaining to NT are readily accessible in the outpatient department (OPD) registers, surveillance registers, and immediate report forms of the EPI surveillance system. The flow of surveillance reports (i.e., weekly and monthly) is from the health facility level to the office of the Executive District Health Officer to the provincial EPI office and finally to the federal EPI cell.[14,70–72] The provincial EPI cell is responsible for the dissemination of information to the district health managers through monthly surveillance reports, and the current system encourages the participation of pediatricians, physicians, and the private sector in disease notification.[70–72] Each health facility level should report a suspected NT case on the immediate report form to the district health office. At the health facility level, each reported NT case is supposed to be entered in the OPD register from which all the cases are abstracted to prepare a monthly surveillance report. At the district health office, the data are 'line-listed'.

Clinical signs and symptoms should be recorded on a standardized case investigation form including information on gender, disease onset, number of maternal TT vaccine doses, reporting, and demographic details.[68,74] The global elimination strategy recommends that case-based surveillance and investigation is vital in districts where TT SIAs have been implemented and where a decline in the number of cases is occurring.[28,74] Beginning July 2009, AFP zero reporting included suspected cases of measles and NT. Zero reporting needs to be meaningful; it should not be seen as a mere absence of cases but as a proxy for active surveillance.

Our experience suggests that the routine analysis of NT surveillance data and the monitoring of the surveillance indicators of completeness and timeliness of reports, and the timeliness of notification to guide program activities at the district level, should be enhanced. We recognize that these indicators can be readily estimated from the surveillance data and are not subject to the inconsistency of a denominator. They have been selected on the basis of precise definitions, policy relevance, simplicity, sensitivity, and time-series data.[75] Nevertheless, there is an urgent need to establish criteria by which to evaluate these indicators so that they can be monitored routinely in a similar manner to the polio indicators.

It is recommended that during active surveillance, health records and vital events registers should be reviewed periodically (for example, once every 2 weeks).[74] This involves searching actively for suspected NT cases in high-risk districts, especially in 'silent' areas where routine surveillance is unreliable or not taking place at all.[74] Surveillance staff have been adequately trained to use the standard case definition[68] to suspect NT during routine reviews of infant deaths and illness.

Inadequate reviews of medical records may contribute to the problem of underreporting of NT, as cases may go undetected and therefore unreported. One study on the NT incidence in Pakistan found that using active surveillance and register reviews, an additional 134 cases were found retrospectively.[20] These were cases that were not routinely reported by the health care professionals as NT cases.[20] Although the study did not explore the reasons for failure to report, it has been hypothesized that workers may still fear the consequences of reporting.[76] Unreported NT cases that are identified during reviews of medical records should be ascertained using the WHO standard case definition[68] and checked if they have not been line-listed in the surveillance register. Effective implementation of a 'high-risk' elimination strategy will continue to depend on enhanced NT surveillance and good immunization data to accurately monitor disease trends and identify those populations and areas where the ongoing risk of NT is still high.

5.3. Inter-sector collaboration/partnerships

Because the majority of NT cases occur in rural areas and hospitals, there has been an increasing effort to expand the reporting sites to include the private sector.[19] This includes private hospitals, clinics, and non-governmental organizations (NGOs) in rural and urban areas. Some of these sources are already obtaining their vaccine stocks from the EPI and provide immunization data to the EPI, so it should not be difficult to enlist their support. Reporting sites should be prioritized based on the identification of high-risk areas, representativeness, health-seeking behavior, the diversity and size of the population, and appropriateness of the designated facility.

Expanding private sector reporting to involve not only the pediatricians in the urban areas but also the physicians and pediatricians in the rural areas may be useful to improve reporting.[19] An active promotion of private sector participation and strengthening of the government sector as a way of improving NT reporting and surveillance has previously been suggested.[20,76] Provision of an adequate supply of resources for reporting, provision of regular feedback from the health authority to health care workers, and the availability and widespread use of birth attendant logs, vital events registries, and standard case definitions in hospitals and private reporting sites may also impact NT reporting and surveillance.[20]

5.4. Community-based NT reporting: role of the LHWs

In Pakistan, not much has been done using community informants and village volunteers to report suspected NT cases and other vaccine preventable diseases. Using health volunteers to report communicable disease outbreaks has been shown to be effective in Cambodia.[77]

The LHW program of the National Programme for Family Planning and Primary Health Care has been found to be effective in delivering family planning and immunization services, as well as the management of diarrhea.[78] The success of the LHW program is primarily due to the unlimited access to households, free interaction with local women, and most importantly the acceptability of LHWs in the communities.[79] LHWs were able to change the poor health care-seeking behavior of women in rural Pakistan.[79] A pilot study by Bhutta et al.[60] found that a community-based intervention for improving perinatal care using LHWs and traditional birth attendants (TBAs) in villages in rural Pakistan was effective in reducing stillbirths and neonatal mortality rates. The intervention consisted of focused training of LHWs in home-based newborn care, training TBAs in basic newborn care and community mobilization, and group education

sessions. In the intervention village, antenatal check-ups during the last pregnancy was greater (79.2%) than in the control village (65.9%) following the intervention, which may have consequently led to an increase in TT immunization during pregnancy in the intervention village (78.5% vs. 65.5%).[60] Overall, the intervention reduced neonatal mortality from a baseline of 52.3 per 1000 live-births to 41.3 per 1000 live-births, whereas the neonatal mortality rate in the control group increased from 52.2 per 1000 live-births to 59.8 per 1000 live-births. To improve TT coverage, immunization programs should be coupled with the LHW program, and should be implemented as a training core in the curriculum of LHWs.[60]

5.5. Methodological issues related to completeness of ascertainment for NT reporting systems

The current experience with NT reporting and surveillance in developing countries has highlighted questions about the adequacy of reporting and the usefulness of surveillance in monitoring the incidence of NT. Underreporting of NT cases may limit the impact of surveillance on the NT elimination efforts. The development of effective surveillance through correct and accurate reporting will not only help to target and evaluate interventions,[3] but will also replace the survey method for obtaining morbidity and mortality data for NT.[12]

Although the current reporting system substantially underestimates the true number of cases, the two-source capture–recapture method was recently used to evaluate case ascertainment in the routine surveillance system and to estimate the incidence of NT in Dadu District, Pakistan.[19,20] Several reporting sources were used with this method: NT surveillance line-list, case records, and registers in government hospitals, and case records and registers from private reporting sites. The most common source of NT reports, routine surveillance, accounted for only 67% of total reports.[20] The proportions of cases reported were 68.1% for government hospitals and 53.8% for private reporting sites; 87% of the unreported cases resided in rural areas.[20] Using the two-source capture–recapture method, overall completeness of routine reporting was 59% for 1993 through 2003,[20] and the average annual incidence was 0.62 per 1000 live-births for the same period.[19] Relative to active case finding, which is the common method for case validation, capture–recapture was a useful and less costly way to assess completeness of reporting routinely.[80] However, there are several limitations and assumptions inherent in the use of the capture–recapture method.[81,82]

Methodological issues related to NT reporting and surveillance that need to be addressed include but are not limited to classification of NT according to the WHO recommended case definition, retrospective hospital reviews of case reports and registers, specifically admission and discharge diagnoses of the cases, and numerator and denominator data. Other sources of data that might be useful for case ascertainment of NT are the DMIS and reporting by community volunteers, LHWs, and TBAs. Cases reported by the latter groups need further validation using the WHO standard case definition[68,83] and/or by a physician to ensure cases are correctly classified. The NT case definition is highly sensitive; however, the sensitivity of the surveillance system is low due to underreporting.[19,84] Routine surveillance data may provide reliable estimates of NT incidence and completeness of reporting when the majority of reporting sources are enhanced and accounted for, which will then feed into the active surveillance system. The increase in routinely reported NT cases from 2005 (Figure 2) may be attributed to the use of the AFP/polio infrastructure to strengthen NT reporting.

6. Improving TT vaccination coverage in Pakistan

To improve TT coverage in Pakistan, changes must be made at the individual, community, and national level. At the individual level, support should be provided by health care workers to childbearing women and their families to ensure that they have an understanding of NT and TT vaccination. Women must be aware of the risks and benefits of vaccination and make an informed decision for themselves and their families. At the community level, LHWs and TBAs are pivotal in improving TT coverage as they are both health care professionals and community members who may also be mothers. Many women seek help from TBAs during pregnancy.[60] Improvements in TBA training in the form of education regarding TT vaccination and safe cord and delivery practices would help to reduce NT incidence. By providing comprehensive training to TBAs, they will be able to educate their clients about safe health care practices for themselves and their families. LHWs can impart knowledge regarding vaccination to women of childbearing age in their communities.[56] This can be accomplished through focus group discussions[85] and community meetings[60] to discuss the benefits of vaccination, under the ideology that women informing and educating other women is powerful. In addition, community-based education is vital in strengthening the socioeconomic status and literacy level of women.[86] While increased knowledge does not necessarily change behavior, Afridi et al. found that females lacking knowledge regarding TT vaccination were less likely to be vaccinated than those who were knowledgeable.[49]

At the national and international level, immunization programs need funding for infrastructure, purchase of vaccines, logistics, and adequate staffing. Attention should be focused on the reasons behind why women fail to receive TT vaccinations. For example, Siddiqi et al. found some women reported not receiving the vaccination due to a lack of understanding of the benefit, distant vaccination centers, misunderstanding of the fear of pain arising from the vaccine, and harm to the fetus.[53] The majority of the reasons for not receiving the vaccination appear to arise from misunderstanding and a lack of adequate knowledge, rooting from the illiteracy of the population.[53] Intensive health education, awareness of the risk of NT, and TT vaccination of women of childbearing age should be targeted to the high-risk districts. To successfully eliminate NT, changes must be made to all three agents of socialization.

7. Strengths and limitations

This study is beset with several limitations including incomplete NT reporting, as cases from the private sector and rural areas are underreported, underestimation of cases due to the failure of health care professionals to report cases, and the use of out-of-date data sources for mortality and TT vaccination coverage surveys not reflecting the current status of TT vaccination. Strengths of the NT elimination program in Pakistan include enhanced reporting and surveillance due to the polio eradication initiative. Routine surveillance of NT cases is improving due to increased intersector collaboration/partnerships, and an increase in TT vaccination coverage in Pakistan has resulted from enhanced elimination activities. The use of multiple data sources allows for a comprehensive assessment of the current NT elimination activities in Pakistan.

8. Conclusions

Our study identified low TT vaccination coverage as the primary driver of neonatal tetanus in Pakistan. Pakistan has made rapid progress over the last decade in increasing TT vaccination coverage

from 60% in 1999 to 74% by the end of 2010. To sustain the progress and efforts made so far, it would be cost-effective to focus limited surveillance resources on monitoring routine TT vaccination coverage with the goal of bringing coverage to the WHO recommended standard. It is expected that by building awareness and understanding of the benefits of TT vaccination, this will provide support and engage the whole community in the integration of health education and related promotional materials into everyday life. It is imperative that the private and government sectors work cooperatively to report NT cases and improve routine TT vaccination coverage.

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References

1. Roper MH, Vandelaer JH, Gasse FL. Maternal and neonatal tetanus. *Lancet* 2007;**370**:1947–59.
2. Schofield F. Selective primary health care: strategies for control of disease in the developing world. XXII. Tetanus: a preventable problem. *Rev Infect Dis* 1986;**8**:144–56.
3. Vandelaer J, Birmingham M, Gasse F, Kurian M, Shaw C, Garnier S. Tetanus in developing countries: an update on the Maternal and Neonatal Tetanus Elimination Initiative. *Vaccine* 2003;**21**:3442–5.
4. Swaddiwudhipong W, Warintrawat S, Kunasol P, Sangwanloy O. Surveillance of neonatal tetanus in Thailand, 1977–1986. *J Med Assoc Thai* 1989;**72**:638–42.
5. Expanded Programme on Immunization. Global Advisory Group—part II. Achieving the major disease control goals. *Wkly Epidemiol Rec* 1994;**69**:29–31. 34–5.
6. Fikree FF, Azam SI, Berendes HW. Time to focus child survival programmes on the newborn: assessment of levels and causes of infant mortality in rural Pakistan. *Bull World Health Organ* 2002;**80**:271–6.
7. Quddus A, Luby S, Rahbar M, Pervaiz Y. Neonatal tetanus: mortality rate and risk factors in Loralai District, Pakistan. *Int J Epidemiol* 2002;**31**:648–53.
8. World Health Organization. Maternal and neonatal tetanus elimination by 2005: strategies for achieving and maintaining elimination. Geneva: WHO; 2000 Available at:http://www.unicef.org/health/files/MNTE_strategy_paper.pdf (accessed March 2011).
9. World Health Organization. Maternal and neonatal tetanus (MNT) elimination: progress towards global maternal and neonatal tetanus elimination. Geneva: WHO; 2011 Available at:http://www.who.int/immunization_monitoring/diseases/MNTE_initiative/en/index4.html (accessed March 2012).
10. Expanded Programme on Immunization. Validation of neonatal tetanus elimination in the Congo by a lot quality-assurance cluster sample survey. *Wkly Epidemiol Rec* 2009;**84**:470–6.
11. Expanded Programme on Immunization. The use of survey data to supplement disease surveillance. *Wkly Epidemiol Rec* 1982;**57**:361–2.
12. Stanfield JP, Galazka A. Neonatal tetanus in the world today. *Bull World Health Organ* 1984;**62**:647–69.
13. Whitman C, Belgharbi L, Gasse F, Torel C, Mattei V, Zoffmann H. Progress towards the global elimination of neonatal tetanus. *World Health Stat Q* 1992;**45**:248–56.
14. Expanded Programme on Immunization Pakistan. National plan of action for maternal and neonatal tetanus elimination in Pakistan. Pakistan: Ministry of Health; 2002.
15. World Health Organization. Expanded Programme on Immunization. The global elimination of neonatal tetanus: progress to date. *Wkly Epidemiol Rec* 1993;**68**:277–82.
16. World Health Organization. Progress towards the global elimination of neonatal tetanus, 1990–1998. *Wkly Epidemiol Rec* 1999;**74**:73–80.
17. World Health, Organization. Maternal and neonatal tetanus (MNT) elimination. The initiative and challenges. Geneva: WHO; 2011 Available at:http://www.who.int/immunization_monitoring/diseases/MNTE_initiative/en/index.html (accessed March 2012).
18. Black RE, Cousens S, Johnson HL, Lawn JE, Rudan I, Bassani DG, et al. Global, regional, and national causes of child mortality in 2008: a systematic analysis. *Lancet* 2010;**375**:1969–87.
19. Lambo J, Khahro Z, Memon M, Lashari M. Neonatal tetanus incidence in Dadu District, Pakistan, 1993–2003. *Scand J Infect Dis* 2011;**43**:175–80.
20. Lambo JA, Khahro ZH, Memon MI, Lashari MI. Completeness of reporting and case ascertainment for neonatal tetanus in rural Pakistan. *Int J Infect Dis* 2011;**15**:e564–8.
21. World Health Organization Pakistan. Expanded Programme on Immunization programme objectives. Pakistan: World Health Organization; 2006 Available at:http://www.emro.who.int/countries/pak/en/ (accessed August 2012).
22. World Health Organization Regional Office for the Eastern Mediterranean. Progress report on globally targeted diseases for elimination: tuberculosis, measles, leprosy and neonatal tetanus. EM/RC53/INF.DOC.7. Egypt: EMRO; 2006.
23. Vandenbroucke JP, von Elm E, Altman DG, Gotzsche PC, Mulrow CD, Pocock SJ, et al. Strengthening the Reporting of Observational Studies in Epidemiology (STROBE): explanation and elaboration. *Epidemiology* 2007;**18**:805–35.
24. Galazka A, Birmingham M, Kurian M, Gasse F. Tetanus. In: Murray JL, Lopez AD, Mathers CD, editors. *Global epidemiology of infectious diseases*. Geneva: World Health Organization; 2004. p. 151–99.
25. Bennett J, Macia J, Traverso H, Banoagha S, Malooly C, Boring J. Protective effects of topical antimicrobials against neonatal tetanus. *Int J Epidemiol* 1997;**26**:897–903.
26. World Health Organization. Tetanus vaccine. WHO position paper. *Wkly Epidemiol Rec* 2006;**81**:198–208.
27. Harfouche JK. The epidemiology of neonatal tetanus. *Pak Pediatr J* 1982;**6**:69–102.
28. World Health Organization. The "high risk" approach: the WHO-recommended strategy to accelerate elimination of neonatal tetanus. *Wkly Epidemiol Rec* 1996;**71**:33–6.
29. Nigam P, Goyal B, Tandon VK, Misra DC, Singh AP, Vajpeyi GN. Tetanus neonatorum—a clinical study of 72 cases. *Indian J Pediatrics* 1974;**41**:135–43.
30. Galazka A. Control of neonatal tetanus. *Indian J Pediatr* 1985;**52**:329–41.
31. Khan SR, Jalil F, Zaman S, Lindblad BS, Karlberg J. Early child health in Lahore, Pakistan: X. Mortality. *Acta Paediatr Suppl* 1993;**82**(Suppl 390):109–17.
32. Suleman O. Mortality from tetanus neonatorum in Punjab (Pakistan). *Pak Pediatr J* 1982;**6**:152–83.
33. Lambo J, Memon M, Khahro Z, Lashari M. Epidemiology of neonatal tetanus in rural Pakistan. *J Pak Med Assoc* 2011;**61**:1099–103.
34. Raza SA, Akhtar S, Avan BI, Hamza H, Rahbar MH. A matched case–control study of risk factors for neonatal tetanus in Karachi, Pakistan. *J Postgrad Med* 2004;**50**:247–51.
35. Katz J. The challenges of eliminating neonatal tetanus. *J Postgrad Med* 2004;**50**:252.
36. Bennett J, Azhar N, Rahim F, Kamil S, Traverso H, Killgore G, et al. Further observations on ghee as a risk factor for neonatal tetanus. *Int J Epidemiol* 1995;**24**:643–7.
37. Bennett J, Schooley M, Traverso H, Agha SB, Boring J. Bundling, a newly identified risk factor for neonatal tetanus: implications for global control. *Int J Epidemiol* 1996;**25**:879–84.
38. Traverso HP, Bennett JV, Kahn AJ, Agha SB, Rahim H, Kamil S, et al. Ghee applications to the umbilical cord: a risk factor for neonatal tetanus. *Lancet* 1989;**1**:486–8.
39. Daud S, Mohammad T, Ahmad A. Tetanus neonatorum (a preliminary report of assessment of different therapeutic regimens). *J Trop Pediatr* 1981;**27**:308–11.
40. Davies-Adetugbo AA, Torimiro SE, Ako-Nai KA. Prognostic factors in neonatal tetanus. *Trop Med Int Health* 1998;**3**:9–13.
41. Pan American Health Organization. Neonatal tetanus elimination field guide, Second ed., Washington: PAHO; 2005.
42. Chai F, Prevots DR, Wang X, Birmingham M, Zhang R. Neonatal tetanus incidence in China, 1996–2001, and risk factors for neonatal tetanus, Guangxi Province, China. *Int J Epidemiol* 2004;**33**:551–7.
43. World Health Organization. Pakistan reported immunization coverage. WHO vaccine-preventable diseases: monitoring system 2011 global summary. Geneva: WHO; 2011 Available at:http://apps.who.int/immunization_monitoring/en/globalsummary/timeseries/tscoveragebycountry.cfm?C=PAK (accessed March 2012).
44. World Health Organization. Pakistan reported cases. WHO vaccine-preventable diseases: monitoring system 2011 global summary. Geneva: WHO; 2011 Available at:http://apps.who.int/immunization_monitoring/en/globalsummary/timeseries/tsincidencebycountry.cfm?C=PAK (accessed March 2012).
45. World Health Organization. WHO vaccine-preventable disease monitoring system, 2010 global summary. WHO/IVB/2010. Geneva: WHO; 2010.
46. Traverso HP, Kamil S, Rahim H, Samadi AR, Boring JR, Bennett JV. A reassessment of risk factors for neonatal tetanus. *Bull World Health Organ* 1991;**69**:573–9.
47. Bennett J, Breen C, Traverso H, Agha SB, Macia J, Boring J. Circumcision and neonatal tetanus: disclosure of risk and its reduction by topical antibiotics. *Int J Epidemiol* 1999;**28**:263–6.
48. Bennett J, Ma C, Traverso H, Agha SB, Boring J. Neonatal tetanus associated with topical umbilical ghee: covert role of cow dung. *Int J Epidemiol* 1999;**28**:1172–5.
49. Afridi NK, Hatcher J, Mahmud S, Nanan D. Coverage and factors associated with tetanus toxoid vaccination status among females of reproductive age in Peshawar. *J Coll Physicians Surg Pak* 2005;**15**:391–5.
50. Zeb A, Zaidi SA, Jehan I. Knowledge, attitude and practices of reproductive age females about tetanus toxoid vaccine: a pilot study. *J Coll Physicians Surg Pak* 2006;**16**:791–3.
51. Hasnain S, Sheikh NH. Causes of low tetanus toxoid vaccination coverage in pregnant women in Lahore district, Pakistan. *East Mediterr Health J* 2007;**13**:1142–52.

52. Ismali K, Sarmad R, Akram Ch M. Assessment of knowledge about prophylaxis of neonatal tetanus among traditional birth attendant. *Biomedica* 2007;**23**:27–30.
53. Siddiqi N, Khan A, Nisar N, Siddiqi AE. Assessment of EPI (expanded program of immunization) vaccine coverage in a peri-urban area. *J Pak Med Assoc* 2007;**57**:391–5.
54. Ayaz A, Saleem S. Neonatal mortality and prevalence of practices for newborn care in a squatter settlement of Karachi, Pakistan: a cross-sectional study. *PLoS One* 2010;**5**:e13783.
55. Nisar N, Aziz N, Mumtaz F. Tetanus toxoid vaccination coverage among pregnant women at tertiary care hospital, Sindh Pakistan. *Medical Channel* 2010;**16**:272–5.
56. Qadir M, Murad R, Mumtaz S, Azmi AA, Rehman R, Omm-E-Hani. et al. Frequency of tetanus toxoid immunization among college/university female students of Karachi. *J Ayub Med Coll Abbottabad* 2010;**22**:147–9.
57. Kashiba Y. Cross sectional study on factors associating neonatal tetanus immunization among reproductive aged women in Kasur District of Punjab Province, Pakistan; mothers' perceived belief on neonatal tetanus and tetanus toxoid vaccination. *J Natl Inst Public Health* 2007;**56**:418–9.
58. Sheikh GA. Neonatal tetanus in Pakistan. *J Trop Pediatr* 1991;**37**:88–9.
59. Griffiths UK, Wolfson LJ, Quddus A, Younus M, Hafiz RA. Incremental cost-effectiveness of supplementary immunization activities to prevent neonatal tetanus in Pakistan. *Bull World Health Organ* 2004;**82**:643–51.
60. Bhutta ZA, Memon ZA, Soofi S, Salat MS, Cousens S, Martines J. Implementing community-based perinatal care: results from a pilot study in rural Pakistan. *Bull World Health Organ* 2008;**86**:452–9.
61. Jehan I, Harris H, Salat S, Zeb A, Mobeen N, Pasha O, et al. Neonatal mortality, risk factors and causes: a prospective population-based cohort study in urban Pakistan. *Bull World Health Organ* 2009;**87**:130–8.
62. National Institute of Population Studies (NIPS) Pakistan, aMII. Pakistan demographic and health survey 1990–91. Islamabad, Pakistan: National Institute of Population Studies and Macro International Inc.; 1992.
63. Federal Bureau of Statistics, Pakistan. Pakistan social and living standards measurement survey 2004–2005. Islamabad, Pakistan: Federal Bureau of Statistics; 2005.
64. Federal Bureau of Statistics, Pakistan. Pakistan social and living standards measurement survey 2005–2006. Islamabad, Pakistan: Federal Bureau of Statistics; 2007.
65. National Institute of Population Studies (NIPS) Pakistan, aMII. Pakistan demographic and health survey 2006–07. Islamabad, Pakistan: National Institute of Population Studies and Macro International Inc.; 2008.
66. Federal Bureau of Statistics, Pakistan. Pakistan social and living standards measurement survey 2006–2007. Islamabad, Pakistan: Federal Bureau of Statistics; 2007.
67. Federal Bureau of Statistics, Pakistan. Pakistan social and living standards measurement survey 2008–2009. Islamabad, Pakistan: Federal Bureau of Statistics; 2009.
68. World Health Organization. WHO-recommended standards for surveillance of selected vaccine-preventable diseases. Geneva: WHO; 2003.
69. Smucker CM, Simmons GB, Bernstein S, Misra BD. Neo-natal mortality in South Asia: the special role of tetanus. *Popul Stud (Camb)* 1980;**34**:321–35.
70. Directorate General Health Services. State of health in Sindh: provincial HMIS feedback report. Sindh, Hyderabad: DGHS; 2003.
71. Directorate General Health Services. HMIS: Reporting trends in Sindh Province. An overview of HMIS data quality and quantity. Sindh, Hyderabad: DGHS; 2002.
72. Directorate General Health Services. Health information for decision making: provincial HMIS feedback report. Sindh, Hyderabad: DGHS; 2004.
73. Vandelaer J, Partridge J, Suvedi BK. Process of neonatal tetanus elimination in Nepal. *J Public Health (Oxf)* 2009;**31**:561–5.
74. World Health Organization. Field manual for neonatal tetanus elimination. WHO/V&B/99.14. Geneva, Switzerland: WHO; 1999.
75. World Health Organization. Communicable disease surveillance and response systems. Guide to monitoring and evaluating. WHO/CDS/EPR/LYO/2006.2. Geneva, Switzerland: WHO; 2006.
76. John TJ, Samuel R, Balraj V, John R. Disease surveillance at district level: a model for developing countries. *Lancet* 1998;**352**:58–61.
77. Oum S, Chandramohan D, Cairncross S. Community-based surveillance: a pilot study from rural Cambodia. *Trop Med Int Health* 2005;**10**:689–97.
78. Oxford Policy Management (OPM). Lady health workers programme—external evaluation of the National Programme for Family Planning and Primary Health Care, 1st ed., Islamabad, Pakistan: Oxford Policy Management; 2002.
79. Hafeez A, Mohamud BK, Shiekh MR, Shah SA, Jooma R. Lady health workers programme in Pakistan: challenges, achievements and the way forward. *J Pak Med Assoc* 2011;**61**:210–5.
80. Hall HI, Song R, Gerstle III JE, Lee LM. Assessing the completeness of reporting of human immunodeficiency virus diagnoses in 2002–2003: capture–recapture methods. *Am J Epidemiol* 2006;**164**:391–7.
81. Brenner H. Use and limitations of the capture–recapture method in disease monitoring with two dependent sources. *Epidemiology* 1995;**6**:42–8.
82. Prevots DR, Sutter RW, Strebel PM, Weibel RE, Cochi SL. Completeness of reporting for paralytic poliomyelitis, United States, 1980 through 1991. Implications for estimating the risk of vaccine-associated disease. *Arch Pediatr Adolesc Med* 1994;**148**:479–85.
83. Cutts FT, Waldman RJ, Zoffman HM. Surveillance for the Expanded Programme on Immunization. *Bull World Health Organ* 1993;**71**:633–9.
84. Singh J, Datta KK, Foster SO. Sensitivity of neonatal tetanus surveillance system in India. *Indian Pediatr* 1997;**34**:398–401.
85. Mansuri FA, Baig LA. Assessment of immunization service in perspective of both the recipients and the providers: a reflection from focus group discussions. *J Ayub Med Coll Abbottabad* 2003;**15**:14–8.
86. Nisar N, White F. Factors affecting utilization of antenatal care among reproductive age group women (15–49 years) in an urban squatter settlement of Karachi. *J Pak Med Assoc* 2003;**53**:47–53.