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## 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 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.

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#### 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.<sup>1,2</sup> The disease usually occurs in rural settings with poor access to health facilities.<sup>3,4</sup> 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.<sup>3,4</sup> NT is one of the most underreported diseases<sup>5</sup> and remains a major but preventable cause of infant and neonatal mortality in many developing countries.<sup>6,7</sup>

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.<sup>8</sup> As of February 2012, Pakistan is one of the 34 countries that have not achieved maternal and neonatal tetanus (MNT) elimination.<sup>9</sup> 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.<sup>10</sup> However, progress in global elimination has been delayed due to slow implementation of the recommended strategies.<sup>3,9</sup>

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).<sup>3</sup> 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.<sup>10</sup>

NT remains a public health problem in Pakistan where it is estimated that the current reporting system captures less than 10% of cases.<sup>11-14</sup> In 1988, 10 countries including Pakistan accounted for more than 70% of all NT deaths worldwide and were targeted for focused activities.<sup>15</sup> 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.<sup>16</sup> By the year 2008, the WHO estimated that the global NT mortality had declined to 59 000,<sup>17,18</sup> a 92% reduction from the situation in the late 1980s.<sup>17</sup> 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.<sup>19</sup> Nevertheless, underreporting of NT remains a public health concern for global elimination and hinders effective surveillance.<sup>19,20</sup>

The Government of Pakistan has set the target to eliminate MNT by 2015.<sup>21</sup> 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'.<sup>14</sup> 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.<sup>22</sup> 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.<sup>22</sup> 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).<sup>23</sup> 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.<sup>2</sup> Contamination of the umbilical cord may occur through cutting the cord using an unclean instrument or applying substances containing tetanus spores to the stump.<sup>24</sup> If contamination occurs when the cord is cut or within the next few days, symptoms begin 3–12 days after birth.<sup>3,25</sup> 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,<sup>24</sup> resulting in muscular stiffness and spasms.<sup>24,26</sup>

The geographical location of a given country and its climate influence the incidence of tetanus.<sup>27</sup> The disease often has a focal distribution, consistently occurring in clusters in geographical areas and population groups with poor birth hygiene<sup>28</sup> and where shared behaviors or the environment enhance the risk of cord contamination.<sup>13</sup> 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.*<sup>27</sup>

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.<sup>29–31</sup> 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.<sup>30</sup>

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

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.

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