EPIDEMIOLOGY OF DIPHTHERIA IN GENRAL POPULATION OF BANNU DIVISION AND IDPs OF NORTH WAZIRISTAN AGENCY (NWA), PAKISTAN

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خلاصہ

خناق سانس کی نالی کے اوپری حصے کی ایک سخت اور متعدی بیماری ہے۔اس کا موجب ایک زہریلا گرام پازیٹو بیکٹریا(Corynebacterium diphtheria)ہے جو تقریباًدس سال سے کم بچوں پر اثرانداز ہوتا ہے۔یہ ترقی پذیر ممالک میں بڑھتی ہوئی شرح اموات اور شرح امراض کی بڑی وجوہات میں سے ایک ہے۔موجودہ تحقیق کا مقصد یہ تھا کہ یہ معلوم کیا جائے کہ ضلع بنوں میں شرح اموات اور اس بیماری کے عام ہونے کی وجوہات کیا ہیں اور اس سلسلے میں ایک ایسی حکمتِ عملی تیار کی جائے کہ مستقبل میں اس بیماری کی روک تھام کے لیے اقدامات کیے جاسکیں۔یہ مطالعہ خلیفہ گلنواز ہسپتال بنوں،ڈسٹرکٹ ہیڈ کوارٹر ہسپتال بنوں اور زنانہ ہسپتال بنوں میں زیر تحقیق لایا گیا۔مختلف عمروں اور جنس کے متاثرہ(مشتبہ) افراد جن کے حلق میں جعلی پردے تھے اور ان کے گلے شدید طور پر متاثر تھے،اس تحقیقی مطالعے کا حصہ تھے۔لیبارٹری تشخیص کے لیے کلچر میڈیا اور Albert's Staining طریقہ کار اختیار کیا گیا۔نتائج سے یہ ظاہر ہوتا ہے کہ شیر خوارگی سے لے کر دس سال کے بچے(76.5%)اس بیماری کی زد میں آسکتے ہیں۔یہ بیماری زیادہ تر ستمبر سے لے کر دسمبر تک غالب رہتی ہے۔اس بیماری کی زیادہ شرح(42%)نومبر کے مہینے میں رپورٹ کی گئی۔اس تحقیق کے دوران 12 اموات رپورٹ ہوئیں۔جن کی شرح 2.8 فیصد بنتی ہے۔اس تحقیق سے یہ نتیجہ اخذ کیا جاسکتا ہے کہ خناق کی بیماری خطرناک حد تک شرح اموات اور شرح امراض کے بڑھنے کا موجب بن سکتی ہے۔اگر بروقت اس کی تشخص اور علاج کی طرف توجہ نہ دی جائے تو یہ ایک خطرناک بیماری ثابت ہوسکتی ہے۔حفاظتی ٹیکے اس جان لیوا بیماری کی روک تھام کا اہم ذریعہ ہیں۔

Abstract

The aim of the current study was to investigate mortality rate and to understand the causes of persistence of diphtheria in Bannu division and to enlighten some strategies to prevent future outbreaks. The study was carried out at District Head Quarter Hospital, Khalifa Gul Nawaz Hospital and Women and Children Hospital of Bannu division. Suspected individuals of various age groups and gender with tender throat and pseudo-membrane were part of this study. Laboratory diagnosis was based on culture media and Albert's staining procedure. Our findings suggest that children of 0-10 years of age group were more vulnerable to diphtheria infection (76.5%). The disease was most prevalent during September to December, 2016; highest incidences were reported in November (n=180, 42%). During the study 12 mortality cases were reported giving the mortality rate of 2.81%.

Introduction

Corynebacterium diphtheriae is the aetiological agent of Diphtheria: an infectious, potentially fatal (Engler *et al*., 2002) upper respiratory tract disease while infrequently affects the skin (Both *et al*., 2014). In 1826 a French pathologist Bretonneau first described diphtheria as a clinical entity. At that time the disease was named as *la diphtherite* by Bretonneau from Greek *diphthera* for membrane, a reference to the "membranes" that appears in the throat of patients (Alcano, 1997). *C. diphtheriae* has four biotypes which are mitis, intermedius, belfanti and gravis (Sangal and Hoskisson, 2016). These are all different in colony morphology and growth characteristics (Kolybo *et al.*, 2013). During respiratory ailment a darkish pseudo-membrane covers the pharynx, tonsils, uvula and the cervical lymph nodes may become tender (Guiso, 2015). *C. diphtheriae* is a gram positive, non-capsulated and aerobic bacteria (Maheriya *et al*., 2014). Children are most frequently affected (Nutan *et al*., 2013) with high morbidity and mortality rates (Guiso, 2015). Transmission may occur through direct contact with case or carrier (Hadfield *et al.*, 2000), respiratory droplets (Nutan *et al*., 21013) or sexual contact (Berger *et al*., 2012). The incubation period is about 2 to 5 days and symptoms may appear up to 10 days after exposure (Phalkey *et al*., 2013). They excrete a locally invasive exotoxin "Diphtheria Toxin" (Dias *et al*., 2011) but the toxic affects extend beyond the local area as it is distributed by the circulatory system. The bacteria has a *tox* structural gene originally found in corynephage virus, the phage incorporates into specific sites in *C. diphtheriae* genome and then its expression is regulated (Hadfield *et al.*, 2000). Diphtheria toxin is an AB-toxin comprised of two subunits; enzymatically active A-subunit and receptor binding B-subunit (Labyntse *et al*., 2014). The toxin blocks protein synthesis by inhibiting EF2 activity (Fattah *et al*., 2013). Worldwide immunization programs against diphtheria significantly reduced incidences of the disease and almost has been eliminated from most of the developed countries. However, Diphtheria is the major health problem in many developing countries of the world including Pakistan.

Materials and Methods

Study area: The current study was performed at District Head Quarter Hospital (DHQ), Khalifa Gul Nawaz Teaching Hospital (KGN), Women and Children Hospital and private clinics of District Bannu after the Ethics Committee approval. The study was conducted from September, 2016 to May 2017.

Data collection: Data was collected from suspected individuals of the Diphtheria disease of Bannu division and IDPs of North Waziristan Agency (NWA) and also from the District Health Office Bannu. A total of 427 individuals (including 264 males and 163 females) were studied. Patients of various age groups and of both sex having fever and sore throat with a greyish white membrane were part of this study.

Laboratory diagnosis

Throat swab: For laboratory diagnosis appropriate clinical specimens were obtained from the throat or naso-pharynx of suspected individuals. Specimens were transported to the laboratory immediately for inoculation of special culture media. For sample collection on swabs and their subsequent transportation to the laboratory, guidelines published by Clarridge *et al*. (1998) and Efstratiou and Maple (1994) were used.

Culture media: The clinical specimens isolated have been grown on blood agar and Hoyle's tellurite medium according to the procedures published (Efstratiou and Maple,1994). Normal oral flora can't grow over the tellurite containing medium, however, *C. diphtheriae* reduces tellurite salts, producing characteristics black colonies (Bisgard *et al*., 1992, Clarridge *et al*., 1998).

Presumptive screening: Albert's staining procedure was performed to demonstrate metachromatic granules in bacteria according to published guidelines (Efstratiou and Maple, 1994).

Results

A total of four hundred and twenty seven (n= 427) cases were studied out of which two hundred and sixty four (n=264, 62%) were male and one hundred and sixty three (n=163, 38%) were female (Fig. 1). The first case of diphtheria was reported on 13th August 2016 of an 8 years old female from Panakzai Kala Miranshah (NWA). The disease reemerged in Bannu division after a long time when IDPs of war against terrorism migrated to Bannu. Initially majority of cases were related to the Panakzai Kala Miranshah of NWA and then the disease was subsequently spread to the local population of Bannu division. During this study 12 mortality cases were recorded giving the mortality rate of 2.81% (including 6 male and 6 female).

Throat swab specimens were collected from the suspected individuals of Diphtheria in D.H.Q Hospital Bannu with the coordination of D.H.O office Bannu. All of them were negative after microscopic examination and bacterial culture technique. Suspected individuals were with greyish white pseudo-membrane in the pharynx.

Gender wise rate of infection of Diphtheria in District Bannu

Total of 255 individuals of diphtheria were reported both from rural and urban areas of Bannu district which is about 59.7% of the total diphtheria cases. Children were more susceptible than adults. Immunization status was the most sticking factor affecting the susceptible to the disease. Among these 153 (60%) were male and 102 (40%) were female (Fig. 2). The most common clinical features were fever and sore throat which were observed in almost all of the infected individuals. Children with myocarditis and temporary paralysis were also observed.

Gender wise rate of infection of Diphtheria in District Lakki Marwat

A total of 45 cases of diphtheria were reported from District Lakki Marwat which is about 10.5% of the total cases. Out of 45 cases, 31 (68.8%) were male individuals and 14 (31.1%) were female (Fig. 3). Children were most common having fever with sore throat and tonsillitis.

Gender wise rate of infection of Diphtheria in NWA

From North Waziristan Agency a total of 127 cases of Diphtheria disease were reported during this study which is about 29.7% of the total cases. Out of 127, there were 86 (67.7%) male and 41 (32.2%) female (Fig. 4). Children were more susceptible. Children with fever and sore throat were common but presented with other complications like myocarditis, pharyngitis and temporary paralysis were also reported.

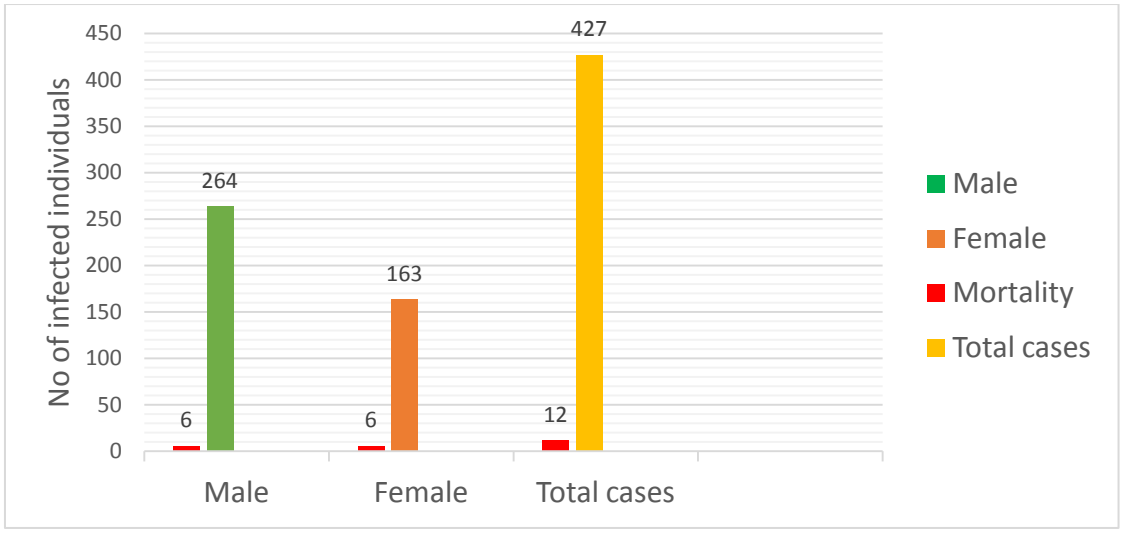

Fig. 1: Overall rate of infection/mortality of Diphtheria in Bannu Division

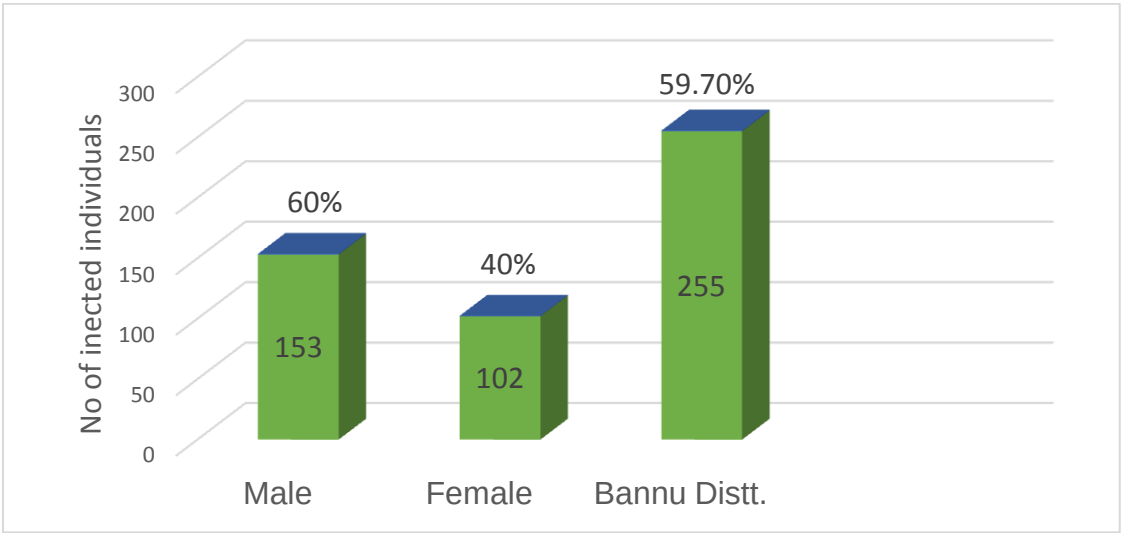

Fig. 2: Infection rate in District Bannu

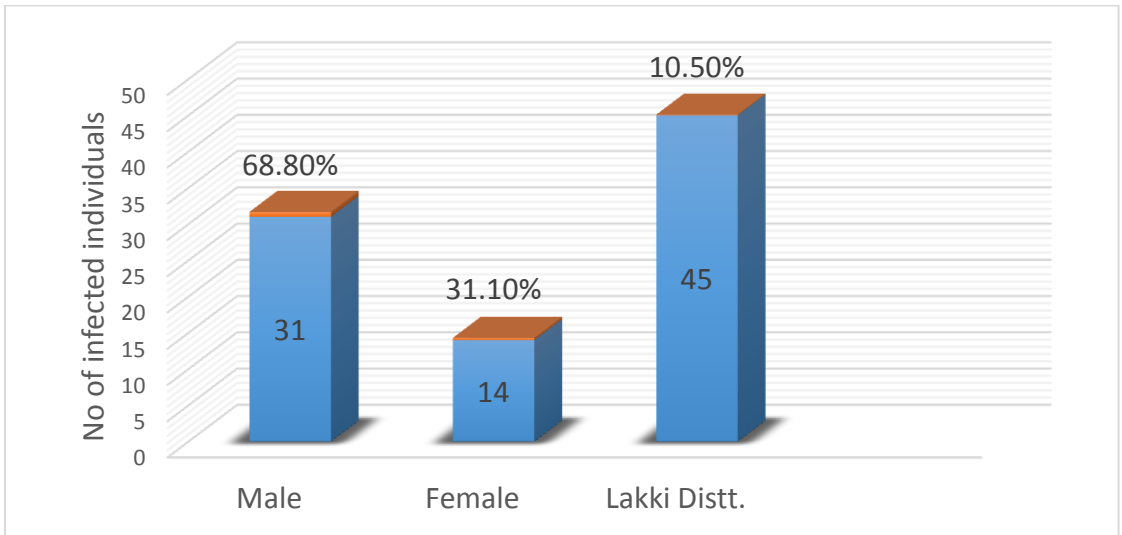

Fig. 3: Infection rate in District Lakki Marwat.

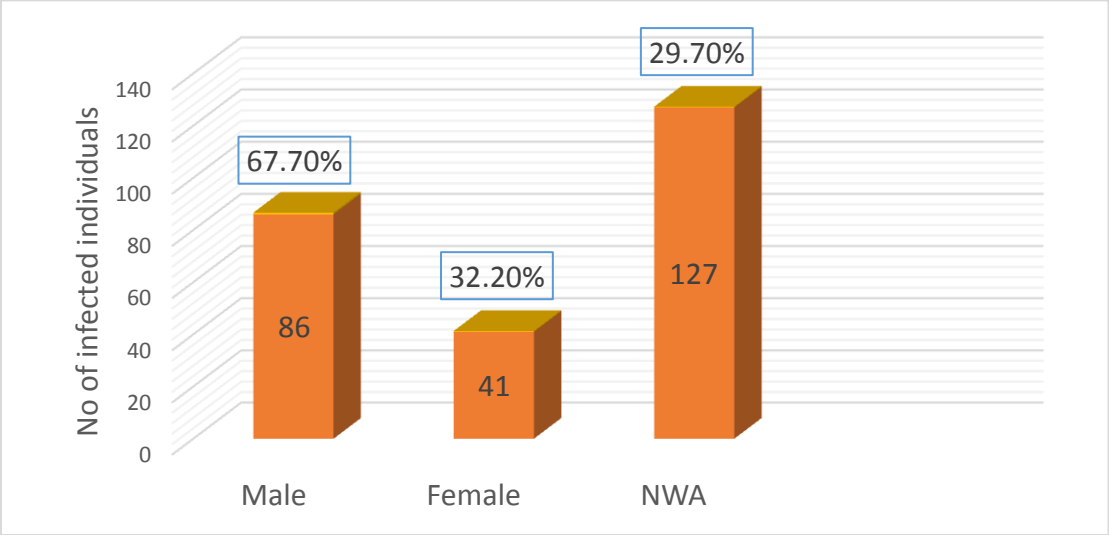

Fig. 4: Infection rate in NWA.

Rate of infection of Diphtheria in different age groups

The total infected individuals of Diphtheria disease were categorized into 3 groups according to their age. The rate of infection of Diphtheria disease was highest (76.5%) in age group of 0-10 years while lowest (1.9%) in age group of 21-30 years (Table 1).

Table 1: Age wise rate of infection of Diphtheria.

S.No.	Age group	Total cases	Percentage
1	0-10	327	76.5
2	11-20	92	21.5
3	21-30	8	1.9

Month wise rate of infection of Diphtheria

Diphtheria disease shows variation from month to month. During this study from September, 2016 to May 2017, a total of 427 individuals were studied. The rate of infection was higher in November, 2016 (42%) while lower (2.5%) in the month of February, 2017. Moreover, no case of Diphtheria disease was reported in March, April and May, 2017 (Table. 2).

Table 2: Month wise rate of infection of Diphtheria

Month	Total cases	Percentage
September	60	14
October	91	21.3
November	180	42
December	73	17
January	12	3
February	11	2.5
March	-	-
April	-	-
May	-	-
Total	427	100

Discussion

In Pakistan the vaccination program against diphtheria was initiated in 1976 and yet there is low level of immunization coverage as 73% to 85% reported in 2008 & 2009 (Faryal *et al.,* 2013). To achieve control over diphtheria in developing countries and Pakistan is still a long way to go.

During the current study a total of 427 suspected individuals of diphtheria disease were studied having sore throat with pseudo-membrane. In this study, no case was positive for *Corynebacterium spp.* in laboratory diagnosis because of early use of antibiotics, the same reason is mentioned by Nutan *et al.*, 2013. Apart from prior usage of antibiotics, lack of skills in sample collection, patient's inability to open their mouth for proper swab collection due to lymphadenopathy and edema/bull neck, resulted in low smear positivity and isolation of microorganisms (Meera and Rajarao, 2014). Besides these, no modern techniques like PCR, update laboratories and skillful lab technicians are available in Bannu division to properly diagnose the disease.

The clinical ailment and its consequences are different in various age groups. Among them the furthermost affected age group was 0-10 years (76.5%) (Table. 1). The current study reveals that there is poor primary immunization in Bannu division for last few decades which needs to be improved to lower the outbreaks of the disease. The possible reasons for low immunization in Bannu division are lack of awareness in people, religious misconceptions, unilateral focus on polio campaigns, avoiding immunization for trivial reasons etc. However, in countries where primary immunization is good the attack rates were highest in age group 10-15 years. A recent epidemic in Assam stated more than 70% of the cases amid 15-45 years of age confirming upward trend for disease (Phalkey *et al.,* 2013).

In recent years many small of moderate outbreaks have taken place from time to time in Bannu division because of low vaccination coverage. This study shows that diphtheria occurs more frequently during the months from September to Decembers. Similar results of diphtheria outbreaks from September to November were reported in India (Meera and Rajarao, 2014). The probable cause may be early monsoon (Sharma *et al.,* 2013). This shows that for early detection of the disease, surveillance in Bannu division should be carried out during the months of August and November.

Diphtheria is associated with high mortality and one of the prognostic factors is the speed with which the antitoxin is administrated. During this study a total of 12 morality cases were confirmed (including male and female) giving the mortality rate of 2.81% (Fig. 1). This mortality rate is very low when compared with the mortality rate (33.3%) recorded in Nigeria and 30.8% in India (Sadoh and Sadoh, 2011). The low mortality rate in our study may be because the data was collected when there was proper vaccine campaigns by health authorities in the area and vaccine containing diphtheria toxoid is the major contributor in bringing down its prevalence and fatality. This recommends that early diagnosis and prompt treatment followed by post or pre-vaccination can diminish fatality rate. To prevent mortality due to diphtheria it is important to achieve universal coverage of DPT vaccine worldwide. At least 80% coverage of DPT is required to control the disease (Maheriya *et al*., 2014).

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