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Original Research

INVESTIGATION OF SUSPECTED PERIPHERAL NEUROPATHY OUTBREAK IN DECHENTSEMO CENTRAL SCHOOL, THINLEYGANG, PUNAKHA

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ABSTRACT
Background: A suspected peripheral neuropathy outbreak was reported from Dechentsemo Central School, Thinleygang, Punakha, following which the investigation team was immediately dispatched in the field.
Objective: The aim of investigation was to ascertain the cause and risk factor for the outbreak in order to implement control measures.
Methods: A case control study was devised for the investigation to study about the past exposure or deficiencies in order to find out the suspected cause and risk factors. A semi-quantitative food frequency questionnaire was administered to both cases and controls to collect information on the type of food they have consumed. The information garnered was analyzed using Chi-Square or Fischer Exact test for categorical variables and Man-Whitney U-test for quantitative variables.
Results: All 17 cases were females with mean age of 13 years (SD 2.7 years). The average daily amount of thiamine intake was 0.6 mg/day for case and 0.8 mg/day for controls against the recommended daily allowance (RDA) of 1.2 mg/day. Case and control patients differed significantly with respect to fat intake (p-value = 0.02), more strongly with folate and iron intake (p-value < 0.01).
Conclusion: The outbreak of peripheral neuropathy in Dechentsemo Central School appears to be linked to reduced dietary intake rich in vitamin B1 coupled with low intake of folate and iron in their diet.

Key Words: Peripheral Neuropathy, Vitamin deficiency, Central School, Bhutan

INTRODUCTION

Nutritional deficiencies are widespread throughout the world which is associated with economic disadvantage and over-crowding.[1] The most commonly described nutritional deficiencies include vitamin B1, vitamin B12, folate, vitamin D, vitamin E and copper deficiencies. Peripheral nervous system is the primary organ affected resulting in peripheral

neuropathy.[2] Peripheral neuropathy results when nerves that carry message to and from brain and spinal cord to rest of the body are damaged or diseased. The debilitating impact of peripheral neuropathy on quality of life and ability to work is considerable and may result in permanent disability.[3] The patients also has high incidence of injuries during walking, limited general functioning and low level of perceived safety.[4]

A suspected peripheral neuropathy outbreak in Dechentsemo Central School in Thinleygang, Punakha was reported to Ministry of Health by Punakha District Health Officer (DHO) on 8th August 2016. A team from Nutrition Program, School Health Program and Royal Center for Disease Control (RCDC) from the Ministry of Health along with the senior officials from the Ministry of Education were immediately deputed to investigate the outbreak.

Dechentsemo Central School is located in Thinleygang, Punakhar district, which is approximately 50km away from the capital. The school has 584 students from which, 268 were male and 316 were female students. The school also provides boarding facilities for some students.

Initially four students who were all girls visited Punakha Hospital on August 6, 2016 with the chief complaint of numbness, weakness and tingling sensation of lower limb. They were all given medication of peripheral neuropathy. On notification of many similar cases by the School Health Coordinator, a team consisting of DHO, District Medical Officer (DMO), Dietician, Laboratory and Pharmacy technicians visited the school for the investigation on August 8, 2016. Additional 13 similar cases were detected on active case finding by the team. A brief health education on peripheral neuropathy was given by DMO and Dietician of Punakha hospital on the same day to the entire students and teachers in the school to stabilize the situation and take preventive measures for the outbreak.

The main objectives of the investigation were:

1. To determine the etiology of outbreak
2. To identify the source of outbreak and population at risk
3. To formulate prevention and control measures to mitigate the number of cases
4. To communicate the result of the investigation to relevant stakeholders

METHODS

Study design

A case control study was devised for the investigation to study about the past exposure or deficiencies in order to find out the suspected causal factors. A case was defined "as any student studying in Dechentsemo Central School, Thinleygang who have manifested tingling sensation in the lower limb, weakness and with or without numbness and cramps". A control referred to "any student who did not show any such signs and symptoms but reside in the same Central School as case at the same time". All cases were included for the study but controls were selected randomly. The past histories and exposures or deficiencies to suspected agents of cases and controls are ascertained retrospectively by direct questioning and with the help of laboratory investigations.

Dietary assessment

A semi-quantitative food frequency questionnaire was administered to both cases and controls to collect information on the type of food they have consumed. The team also checked the diet schedule as maintained by the school mess to gain better insight of the food served to the students. The daily intake of nutrients which includes carbohydrates, fats, protein

and micronutrients were analyzed by submitting the collected dietary information in the Nutrisurvey 2007 software.

Laboratory study

Plasma serum specimens were randomly collected from cases and controls. The specimens were tested for sugar level in the district hospital.

Statistical analysis

Descriptive analyses were presented in frequencies, percentage, mean, standard deviations and graphs. For categorical variables, frequencies with which the same characteristics or exposures are found in the diseased and non-diseased groups are compared with Pearson Chi-square or Fischer Exact test. Associations of quantitative variables with the peripheral neuropathy were assessed by Man-Whitney U test. The magnitudes of risk factors were analyzed using odds ratio and p-value less than 0.05 were considered statistically significant.

Ethical statement

Since the investigation was conducted in response to emergency/outbreak, no ethical clearance was required from Research Ethics Board of Health (REBH), Ministry of Health, Bhutan as a part of routine procedure.

RESULTS

General Characteristics

All 17 cases were females and no male patients were reported in the outbreak. The mean age of cases was 13 years (SD 2.7 years) which ranged from 9-18 years. Almost more than half of the cases and controls have their parents working as farmers (53%). Parents of seven cases were divorced and living with either single parent or with their relatives. Among the cases and controls, seven were vegetarian and three were controls respectively (Table 1).

Table 1 General Characteristics of students with syndrome (cases) and without syndrome (controls) at Dechentsemo Central School, August 2016

General Characteristics	Cases (N=17)	Controls (N=17)	p-value
	Frequency	Frequency	
Female	17	6	0.33*
Age			
Mean ± SD (Years)	13 ± 2.70	12 ± 2.81	0.32**
Mini - Max (Years)	9 - 18	9 - 18	
Occupation of parents			
Civil Servant	0	2	0.39**
Business	3	1	
Plumber + Carpenter + Guard	5	5	
Farmer	9	9	
Marital status of parents			
Into-relationship	10	7	0.30*
Divorced	7	10	
Dietary habits			
Vegetarian	7	3	0.10*
Non-vegetarian	10	14	
*Pearson Chi-Square	**Fisher Exact		

Clinical Characteristics

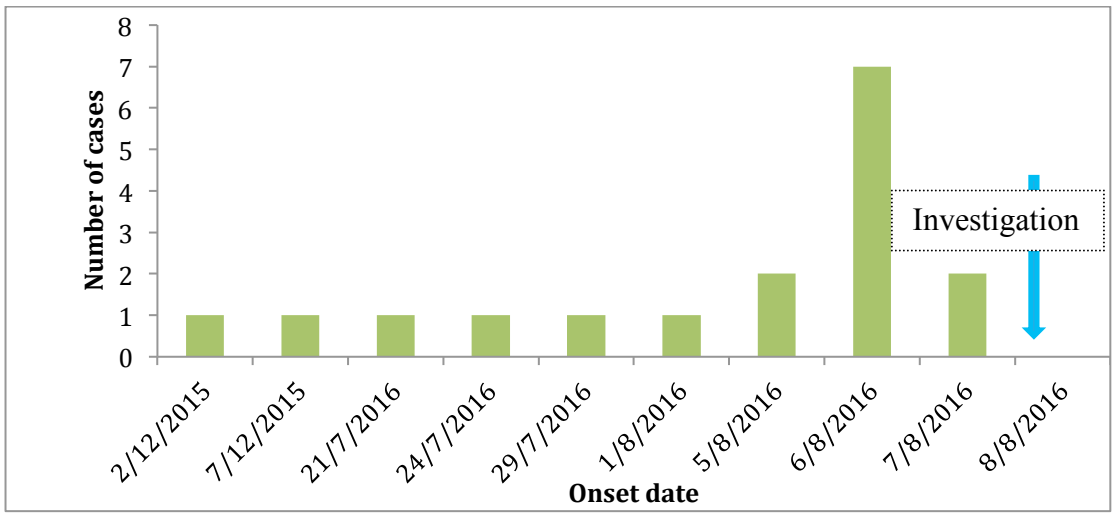
Among the case patients, all of them manifested tingling sensation in the lower limbs, while some showed such symptoms in the upper limbs. Numbness was observed in 14 of them followed by fever, weakness, occasional cramps and limping (Figure 1). The mean blood

pressure and BMI for cases were 108.06/96.01 mm of Hg and 19.5 kg/m² respectively. Similarly mean blood pressure and mean BMI for controls were 80.04/61.20 mm of Hg and 18.3 kg/m² respectively.

Figure 1. Signs and Symptoms of case patients

The date of onset of illness range from 2/12/2015 to 7/8/2016. The outbreak was neither a common source, nor propagated from person to person (Figure 2). The onset of two cases occurred in 2015. The highest case was observed on 6th August, 2016, while other dates represented either one or two cases.

Figure 2. Epidemic curve



Analysis of Risk Factors

On dietary recall by both case and control subjects, no statistical significant difference was found with respect to energy, protein, vitamin B1, vitamin B2, vitamin B6 and zinc intake (p-value > 0.05). However, two groups differed significantly with respect to fat (p-value = 0.02), more strongly with folate and iron intake (p-value < 0.01) (Table 2).

Table 2. Association of quantitative nutritional and laboratory findings with suspected peripheral neuropathy by Man-Whitney U test

Test Parameters	Case	Control	p-value
	Mean Rank (Mean value)	Mean Rank (Mean values)	
Energy(kcal)	16.33 (753.376)	12 (733.811)	0.17
Protein(g)	12.62 (21.27)	13.81 (26.19)	0.71
Fat(g)	10.85 (10.96)	18.5 (19.31)	**0.02**
B1(mg)	11.53 (0.73)	17.22 (0.82)	0.06
B2(mg)	14.18 (0.48)	12.22 (0.47)	0.50
B6(mg)	15.09 (0.89)	10.5 (0.70)	0.13
Folic(mcg)	10.24 (59.90)	19.67 (89.70)	**<0.01**
Iron(mg)	10.59 (5.95)	19 (6.94)	**<0.01**
Zn(mg)	11.91 (4.37)	16.5 (5.51)	0.12
Plasma sugar (mg/dl)	18.12 (110.35)	16.88 (105.58)	0.73

Odds ratio for dietary habit and marital status was calculated to assess their risk pattern for the outcome. From table 3, the odds ratio of 3.26 for vegetarian implies that the vegetarian are 3.26 more likely to develop peripheral neuropathy as compared to non-vegetarian. This magnitude however was non-significant as 95% confidence interval included 1. Odds ratio for those cases whose parents were divorced was 0.49 (95% confidence interval 0.13 – 1.92) as compared to those whose parents are into relationship.

Table 3. Risk analysis for lifestyle of case and control subjects

Risk Factors	Cases (N=17)	Controls (N=17)	Odds Ratio	95% Confidence Interval
Dietary habit				
vegetarian	7	3	3.26	0.67 - 15.82
Non-vegetarian	10	14		
Marital status of parents				
Divorced	7	10	0.49	0.13 - 1.92
Relationship	10	7		

DISCUSSIONS

The investigation provides a clinical description and analysis of risk factor for the peripheral neuropathy outbreak in Dechentsemo Central School. No physical or social activities were conducted in the school prior to outbreak. The foods were served according to the food menu as prepared by the school management. The prominent clinical features among the cases were tingling of the lower limbs followed by numbness, fever, weakness, occasional cramps and limping. Unlike in the past outbreaks, no edema was observed. All these features were suggestive for the diagnosis of peripheral neuropathy as shown in the previous study.[5]

The outbreak is neither a continuous common source nor propagated from person to person. For a continuous common source, the range of exposure and incubation period get flattened and widen the peaks of epidemic curve.[6] In a propagated outbreak, the disease is transmitted from person to person either via a direct contact or through other vehicles. Initially the number of detected cases was consistent over the period from 2/12/2015 to 5/8/2016 with abrupt increase on 6/8/2016. Such a sharp peak is not detectable in continuous common source outbreak. From 8/8/2016, no cases were reported from the school.

In the previous outbreaks which occurred sporadically in different places across the nation, dietary deprivation specifically Vitamin B1 was implicated as the causal factor. The present outbreak also appears to be linked to inadequate intake of diet which may have contributed to the development of neuropathy. The average daily amount of thiamine intake as calculated from their usual menu was 0.6 mg/day for case and 0.8 mg/day for controls against the recommended daily allowance (RDA) of 1.2 mg/day.[7] The preponderance of female patients in the outbreak may reflect a different dietary habit, lifestyle, physical activity and their degree of susceptibility to peripheral neuropathy as compared to males. Previous studies have also shown that females are mostly affected than males.[8] Moreover, controls have significantly higher intakes of folate, fat and iron than case. Although statistically not significant, females tends to be vegetarian than males. Vegetarian are 3.26 times more likely to suffer from peripheral neuropathy than non-vegetarian. The insignificant association presented here might be attributed to very small sample size.

Analyses of specimen for the selected variables do not reveal any significance difference between cases and controls and their values are all within the normal range. Plasma sugar was analyzed for both cases and controls to rule out diabetes. Many studies in the past have demonstrated peripheral neuropathy as a complication of diabetes.[4,9-12]

CONCLUSIONS

The outbreak of peripheral neuropathy in Dechentsemo Central School appears to be linked to reduced dietary intake rich in vitamin B1 which may be caused by different dietary habits, lifestyles and individual susceptibility to peripheral neuropathy. The cases were also found to be associated with low intake of fats, folate and iron in their diet. Students must be encouraged to take balanced diet with green leafy vegetables and meat, especially among females along with supplementation of vitamins.

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