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Risk factors for human cysticercosis morbidity: a population-based case-control study

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SUMMARY

A population-based case-control study to determine social and behavioural risk factors for *Taenia solium* cysticercosis in humans was carried out in a rural area, Shandong province, China. Forty-eight cases with cysticercosis were ascertained through a prevalence survey conducted among 7281 persons in 1993. For each case, four controls residing in the same village and matched for age and sex were randomly selected. Information regarding demographic, social and behavioural factors was collected during house visits through interviews and direct observation. Risk factors strongly associated with human cysticercosis included poor personal hygiene, being unable to recognize cysticerci-containing meat, poor pig-raising practices and a history of passing tapeworm proglottides. The results indicate that health education in combination with chemotherapy for taeniasis is required for the control of cysticercosis in humans.

INTRODUCTION

Taenia solium cysticercosis in humans is a parasitic zoonosis with public health importance in pig-raising communities of developing countries [1]. People can get cysticercosis if they ingest *T. solium* eggs from the environment through contaminated hands, water and food, or from their own tapeworm infection. In human hosts, *T. solium* eggs develop into cysticerci (larval stages) which invade various locations such as skeletal muscle, subcutaneous tissue, eye, etc. Autopsy series and clinical reports have indicated that cysticerci seem to prefer the central nervous system causing neurocysticercosis, which may cause severe and

prolonged neurological dysfunction and sometimes death [2]. As one of six ‘eradicable’ or ‘potentially eradicable’ infectious diseases [3], knowledge of risk factors for the infection is needed to design control programmes, for endemic areas. Studies performed in Latin America suggest that the risk for cysticercosis is associated with human and pig behavioural interaction [4–6]. Despite a wide awareness of the significance of social and behavioural influences on the spread of human cysticercosis, there has been a relative lack of research to assess such factors in China, where cysticercosis causes much suffering. A study was conducted in a rural area of Shandong province in 1992–3. Our previous report provided the serological evidence of human cysticercosis in the community, and explored risks associated with the infection [7]. In the present paper, we conducted a matched case-control study to identify significant

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predictors of morbidity due to cysticercosis using patients with clinical manifestations.

METHODS

A prevalence survey was carried out in 1992–3. Four study teams, each consisting of an epidemiologist, a physician and a health worker conducted door-to-door visits. All residents above 3 years of age ($n = 7281$) in the study area were investigated. Cases of cysticercosis were ascertained through a two-phase approach. First, questions related to the presence of subcutaneous nodules, passing tapeworm proglottides in the stool, and suggestive symptoms of neurological and psychiatric disorders were asked. Blood samples were collected from individuals who were willing to cooperate (2898 persons), and tested for anti-cysticerci antibody [7]. To confirm the presence of nodules and evaluate neurological dysfunction, general examination was performed by a physician. All persons responding positive to one or more of the questions or showing positive results in the initial serological tests were invited to the hospital of the Shandong Institute of Parasitic Diseases, where they were offered free neurological examination, sophisticated laboratory tests, and when necessary, instrumental examination such as CT scan of the brain and biopsy.

Subcutaneous/muscular cysticercosis was defined as palpable cysts or nodules confirmed to be caused by cysticerci on biopsy. Neurocysticercosis was defined if two or more of the following items were found: (1) neurological manifestations, such as epilepsy, intracranial hypertension, hydrocephalus, psychiatric symptoms, etc., without other identified causes; (2) increased cerebrospinal fluid (CSF) pressure, leucocyte count or protein content; (3) a positive result of immunological test (ELISA) on serum or CSF; (4) a typical photographic image of cysticerci in skull CT. All confirmed cases were included in the case-control study.

For each case, four controls living in the same village and matched for age (± 1 year) and sex were randomly selected from those without evidence of cysticercosis and with negative results of serological tests. When less than four controls for a given case were found, the matching for age was broadened to ± 2 years.

Data on demographic characteristics, social status and behavioural patterns were collected for cases and controls at the time of the first contact. Data were recorded on name, age, sex, occupation, education,

village of living, eating habits and diet, food preference, drinking unclean water, presence and structure of latrine, the usual site of defecation, pig ownership, general knowledge related to *T. solium* infection and its causation. Respondents were asked whether they had ever heard of or seen cysticerci-containing pork. If they answered 'Yes' their interviewers showed them specimens of infected and uninfected meat and their ability to discriminate was recorded. Questions were asked based on a structured questionnaire, and data regarding latrine construction and pig-raising practice were obtained by direct observation.

Conditional logistic regression for a matched design [8] was performed using the LogXact-Turbo software package (Cytel Software Corporation, 1993). Odds ratios (OR), their 95% confidence intervals (95% CI) and *P*-values were estimated by maximum likelihood methods. When the asymptotic maximum likelihood method failed to converge, these estimates were obtained using the exact method based on permutational distributions of sufficient statistics [9]. Univariate analysis was conducted to examine the effect of each variable separately. Afterwards multivariate analysis was carried out using a forward stepwise approach to construct a model that included only the variables remaining statistically significant in the presence of other significant variables.

RESULTS

In the prevalence survey, 7281 residents were investigated. Forty-eight cysticercosis patients were detected and used as cases in the present study (Table 1). Of the 48 cases, 31 were diagnosed as neurocysticercosis, 18 of whom also had palpable cysts. The other 17 cases were patients with subcutaneous and muscular cysticercosis. 15 were male and 33 were female. The mean age of cases was 38.2 years (standard deviation [s.d.] = 16.7). Matched analysis showed that occupation of respondents was not associated with cysticercosis ($P = 0.76$). There was no significant association between education and cysticercosis ($P = 0.21$). When the analysis was restricted to the subjects over 20 years of age, who probably had left school, the association was still not significant ($P = 0.18$).

On univariate analysis, six variables were found to be statistically significant ($P \leq 0.05$): poor defecating habit (defecating indiscriminately rather than in a latrine), being unable to recognize cysticerci-con-

Table 1. *Distribution of demographic characteristics of cases and controls*

Character	Cases (<i>n</i> = 48)	Controls (<i>n</i> = 192)
Age (years)		
≤ 19	6 (13)*	24 (13)*
20–	6 (13)	20 (10)
30–	14 (29)	60 (31)
40–	8 (17)	32 (17)
50–	7 (15)	28 (15)
≥ 60	7 (15)	28 (15)
Occupation†		
Pre-school child	2 (4)	10 (5)
Student	4 (8)	14 (7)
Farmer	39 (81)	162 (84)
Factory worker	2 (4)	3 (2)
Other	1 (2)	3 (2)
Education‡		
Pre-school child	2 (4)	10 (5)
Illiterate	15 (31)	50 (26)
Primary school	10 (21)	63 (33)
Secondary school	17 (35)	59 (31)
High school	4 (8)	10 (5)

* Percentages are given in parentheses.

† Exact conditional score test, $P = 0.76$.

‡ Maximum likelihood score test, $P = 0.21$.

taining pork, having a history of passing tapeworm proglottides, raising pigs, allowing pigs to feed on human faeces and using the pigsty as a toilet (Table 2). The six variables with significance in the univariate analyses were further investigated by multiple conditional logistic regression using a forward stepwise approach. The final model in multivariate analysis revealed four factors independently associated with human cysticercosis (Table 2).

DISCUSSION

The principal advantage of our field study is the representativeness of cases and controls for the general population, resulting in findings that are more useful for planning community-based control programmes than findings from hospital-based studies in which results are likely to be biased due to the specific characteristics of hospitalized patients [10]. The information regarding potential risk factors was collected through interviews and direct observation before the diagnosis of cysticercosis was established. Both interviewers and respondents were ignorant of the classification of the respondent as a case or a control. This methodology should reduce bias in the

estimation of exposure to risk factors. However, the study may have suffered from a prevalence–incidence bias, because prevalent cases were used [10]. Prevalent cases represent a past infection. In a case-control study it is difficult to distinguish events preceding or following the infection. However, because the residents in the study area do not change their habits rapidly in time, it can be expected that the social and behavioural patterns found in this study correspond to the conditions at the time of infection.

Another methodological issue concerns the diagnosis of cysticercosis. The present study followed a two-phase diagnostic procedure. If persons were suspected to be positive for cysticercosis after general observation, oral inquiry about presence of symptoms, or serological testing, specific further diagnostic investigations were performed to confirm cysticercosis. This strict protocol minimized the presence of false-positive cases. We did not confirm controls to be disease free but such misclassification bias tends to dilute the association between a risk factor and the disease [8].

Case-control studies are based on the assumption that individual outcomes are independent. For infectious diseases this assumption may pose problems when cases are clustered within houses or neighbourhoods [11]. In the present study, such clustering did not occur.

Other studies [4–6] and our previous paper [7] reported on serological evidence of human cysticercosis. Such data draw attention to the presence of *T. solium* infections in a community, but fail to assess the morbidity due to cysticercosis. The investigation of clinical disease and its risk factors would offer specific and sensible information for health authorities to plan control programmes. The findings of the present paper are in accordance with our previous report on seroprevalence of the same survey [7].

Individuals without knowledge on infected meat have a higher risk of getting taeniasis by misingestion, and may subsequently get cysticercosis. This risk factor is significant for seropositivity as well as cysticercosis morbidity. We anticipate that this factor will remain important in the future. Since the establishment of the free market economy in China, many persons have set up small businesses by selling pork on the local market. At the same time the regulations for meat inspection have become less strict. Presently, meat can be sold without official examination, allowing cysticerci-containing pork to enter the market.

Table 2. Potential risk factors and their association with cysticercosis*

Factor	Cases (n = 48)	Controls (n = 192)	Univariate analysis		Multivariate analysis	
			Crude OR (95% CI)	P	Adjusted OR (95% CI)	P
Eating uncooked vegetables	27 (56)§	120 (63)‡	0.7 (0.4, 1.5)	0.38	—	—
Eating unclean fruit	23 (48)	91 (47)	1.0 (0.5, 2.0)	0.95	—	—
Drinking unclean water	18 (38)	49 (26)	2.1 (0.9, 4.5)	0.07	—	—
Not washing hands after defecation	43 (90)	161 (84)	2.2 (0.6, 7.3)	0.22	—	—
Eating food with dirty hands	38 (79)	132 (69)	1.9 (0.8, 4.4)	0.12	—	—
Poor defecating habit†	47 (98)	97 (51)	36.2 (4.9, 266.4)	< 0.01	33.1 (5.4, 1373.3)	< 0.01
Latrine poorly constructed	21 (44)	67 (35)	1.6 (0.8, 3.2)	0.21	—	—
Raising pigs†	20 (42)	49 (26)	2.6 (1.2, 5.7)	< 0.05	Not selected	—
Using pigsty as a toilet†	14 (29)	32 (17)	2.4 (1.0, 5.3)	< 0.05	Not selected	—
Allowing pigs to feed on human faeces†	19 (37)	36 (19)	3.5 (1.6, 7.7)	< 0.01	4.3 (1.3, 17.4)	< 0.05
Being unable to identify diseased meat†	48 (100)	160 (83)	18.4 (2.9, +INF)	< 0.01	11.7 (1.9, +INF)	< 0.01
History of taeniasis†	7 (15)	2 (1.0)	14.0 (2.9, 67.4)	< 0.01	9.2 (1.2, 136.9)	< 0.05

* Calculation is based on the difference between having the risk factor and without risk factor.

† Factors with significance ($P < 0.05$) in univariate analysis, were included in the model of multivariate analysis using a forward stepwise approach.

‡ Percentages are given in parentheses in these columns.

Defecating indiscriminately rather than in a toilet is also identified as a risk factor for cysticercosis seropositivity as well as morbidity. Individuals with such poor defecating habit generally have poor hygienic behaviours, and thus run a high risk of cysticercosis and other helminthic infections.

As also noted in studies carried out in Latin American countries [5, 6], our study found that a history of taeniasis (passing tapeworm proglottides) is a prominent predictor for cysticercosis morbidity. Since there is no *Taenia saginata* (beef tapeworm) present in the province, the finding indicates that auto-infection may be an important way of getting cysticercosis in humans.

Raising pigs, allowing pigs to feed on human faeces and using the pigsty as a toilet are household-related variables, which are correlated. Allowing pigs to feed on human faeces is an independent risk factor for cysticercosis morbidity, whereas raising pigs is independently associated with seropositivity [7]. Although the results are not exactly consistent, they confirm that cysticercosis is associated with pig ownership and pig-raising practice. In the study area, pigs are raised in households, and most are permitted to scavenge human faeces. Such a feeding method not only causes high risk of porcine infection, but also favours the transmission of human cysticercosis in the community because the pigs help disseminate parasite

eggs in the environment. To assess this factor further, investigation is needed to examine environmental contamination with *T. solium* eggs.

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