**Diabetes and associated disorders in Cambodia: two epidemiological surveys**

Original Text

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**Summary**

**Background**

The Asia-Pacific region is thought to be severely affected by diabetes. However, reliable, standardised data on prevalence and characteristics of glucose intolerance in Asian populations remain sparse. We describe the results of two field surveys undertaken in Cambodia in 2004.

**Methods**

2246 randomly selected adults aged 25 years and older were examined in two communities, one rural (Siemreap) and one semi-urban (Kampong Cham). The diagnosis of diabetes and impaired glucose tolerance was based on 2-h blood glucose estimation using criteria recommended by the latest report of a WHO Expert Group. Blood pressure, anthropometry, habitual diet, and other relevant characteristics were also recorded.

**Findings**

Prevalence of diabetes was 5% in Siemreap and 11% in Kampong Cham. Prevalence of impaired glucose tolerance was 10% in Siemreap and 15% in Kampong Cham. About two-thirds of all cases of diabetes were undiagnosed before the survey. Prevalence of hypertension was 12% at Siemreap and 25% at Kampong Cham. People in Kampong Cham had higher estimates of central obesity than those in Siemreap.

**Interpretation**

Diabetes and hypertension are not uncommon in Cambodia. A quarter of all adults in the chosen suburban community had some degree of glucose intolerance. Since Cambodian society is relatively poor, and lifestyle is fairly traditional by international standards, these findings are unexpected.

**Introduction**

During the past quarter century, diabetes, cardiovascular disease, and obesity have emerged as major causes of morbidity and mortality throughout the world.[1](http://www.thelancet.com/journals/lancet/article/PIIS0140-6736%2805%2967662-3/fulltext%22%20%5Cl%20%22bib1%22%20%5Co%20%22) Although falls in the incidence of cardiovascular disease have been recorded in some industrialised countries,[2](http://www.thelancet.com/journals/lancet/article/PIIS0140-6736%2805%2967662-3/fulltext%22%20%5Cl%20%22bib2%22%20%5Co%20%22) most reports suggest an epidemic of diabetes and obesity, frequently associated with hypertension and hyperlipidaemia in most developed and developing countries. Moreover, in the case of diabetes, the less developed countries seem to be particularly prone,[3](http://www.thelancet.com/journals/lancet/article/PIIS0140-6736%2805%2967662-3/fulltext%22%20%5Cl%20%22bib3%22%20%5Co%20%22) probably because of the adverse effects of rapid socioeconomic transition and accompanying changes in dietary habits and physical activity.[4](http://www.thelancet.com/journals/lancet/article/PIIS0140-6736%2805%2967662-3/fulltext%22%20%5Cl%20%22bib4%22%20%5Co%20%22) The Asia-Pacific region is thought to be severely affected, although reliable data remain sparse.

Cambodia is a tropical southeast-Asian country with a population of 12 million people.[5](http://www.thelancet.com/journals/lancet/article/PIIS0140-6736%2805%2967662-3/fulltext#bib5) Cultivation of rice is the dominant activity in rural areas, which contain 80% of the population of the country. Life expectancy at birth is 54 years for men and 58 years for women. Infant and childhood mortality to age 5 years is 124 per 1000 livebirths,[6](http://www.thelancet.com/journals/lancet/article/PIIS0140-6736%2805%2967662-3/fulltext%22%20%5Cl%20%22bib6%22%20%5Co%20%22) gross national income per head is US$320 per year, country rank 187 in the world.[7](http://www.thelancet.com/journals/lancet/article/PIIS0140-6736%2805%2967662-3/fulltext%22%20%5Cl%20%22bib7%22%20%5Co%20%22) Population growth is 1·8% per year, and adult literacy rate is 74%.[5](http://www.thelancet.com/journals/lancet/article/PIIS0140-6736%2805%2967662-3/fulltext#bib5)

During the final years of the 20th century, Cambodia returned to relative political stability after many years of war and deprivation, and it is now experiencing a degree of economic recovery. The geographical, cultural, and economic conditions within Cambodia are not uniform. Whilst the majority of the population continues to live in rural areas, there are also several towns, in addition to the capital city, Phnom Penh. Lifestyle and ethnicity also differ between different regions of the country. Therefore, to gain a full understanding of the burden of non-communicable diseases for the country as a whole, assessment of several population samples is needed. During 2004, we undertook surveys in two provinces.

**Methods**

**Study populations**

During January, 2004, we did a survey in two rural villages in Siemreap Province in the northwest of the country, near to the shore of Lake Tonle Sap. Two communities were chosen which were judged to be typical of the traditional Khmer-Melanesian culture and lifestyle. The village of Damdek is situated on the northern side of the main national road number 6, about 40 km to the east of Siemreap town. Samrong lies about 10 km to the north of Damdek and is reached by an unpaved road. Therefore, Damdek has easier contact with urban amenities and may have been more affected by recent changes in lifestyle than Samrong. However, in both villages, economic conditions are poor, with little sanitation and no household electricity or running water.

The second survey, of two communities in Kampong Cham Province in the southeast of the country, close to the frontier with Vietnam, was done in June, 2004. Communities in this district are more socioeconomically developed than in Siemreap Province, owing to the historic trade route of the Mekong River, and exposure to Vietnamese, Chinese, and colonial French influences. Khum Boeung Kok is a middle-income suburban district of Kampong Cham township and Khum Veal Vong is one of the most affluent districts of the town, with most residents occupied in commerce and administration.

The project received ethics approval from the Cambodian Ministry of Health. All participants gave verbal consent after the purpose and procedures of the survey had been explained to them. Each participant was informed of his or her status with regard to glucose intolerance, hypertension, and obesity at the end of their examination. People with newly discovered diabetes or hypertension were referred for clinical appraisal.

**Procedures**

Survey methods were those recommended in the WHO field guide for diabetes and non-communicable disease risk factor surveys.[8](http://www.thelancet.com/journals/lancet/article/PIIS0140-6736%2805%2967662-3/fulltext#bib8) A house-to-house census was done before each survey, to compile accurate population lists and to inform participants of the purpose and procedures of the work. During the surveys, about 100 people per day were examined at a central site (usually a village or community health centre).

Diabetes, impaired glucose tolerance, overweight, central obesity, and hypertension were classified according to the most recent WHO recommendations:[9—11](http://www.thelancet.com/journals/lancet/article/PIIS0140-6736%2805%2967662-3/fulltext%22%20%5Cl%20%22bib9) for diabetes, capillary blood glucose concentration of 11·1 mmol/L or greater, 2 h after a 75 g glucose load preceded by at least 8 h fasting; for impaired glucose tolerance, 2-h blood glucose concentration 6·8—11·0 mmol/L; for overweight, body-mass index (BMI) 25·0 kg/m2 or greater; for central obesity, waist-hip ratio 1·0 or greater for men and 0·85 or greater for women; and for hypertension, systolic blood pressure (SBP) 140 mm Hg or greater, and/or diastolic blood pressure (DBP) 90 mm Hg or greater, or being on antihypertensive medication.

Concentration of glucose in blood was measured on site with HemoCue blood glucose analysers (HemoCue AG, Ängelholm, Sweden), which use a glucose dehydrogenase method of estimation. Alternate high and normal standard solutions were tested on each machine after every 20 samples. All readings fell within the range recommended by the manufacturer. Participants currently taking medication for diabetes were classified as being diabetic, and those reporting a previous diagnosis of diabetes but no treatment underwent fasting blood glucose examination. If within the diagnostic range for diabetes, they were classified as diabetic; otherwise, they took the glucose drink to confirm their diabetic status.

BMI, waist-hip ratio, and blood pressures were measured twice in each individual and the mean used for the purpose of analysis. A short questionnaire was administered concerning previous diagnosis of diabetes and hypertension and their treatment, family history of these disorders, habitual diet and physical activity, and tobacco smoking. Cambodian diet is conservative and for all participants the daily staple was rice; therefore, the dietary questions did not relate to this item. Weekly frequencies were sought for the other major food items; meat, fish, fruit, and vegetables. Physical activity was graded on an ordinal scale of 1—4, corresponding to sedentary, light, moderate, or heavy habitual physical activity, according to local standards.[8](http://www.thelancet.com/journals/lancet/article/PIIS0140-6736%2805%2967662-3/fulltext%22%20%5Cl%20%22bib8%22%20%5Co%20%22) For the purpose of data analysis, these results were transformed into a binary variable—inactive (grades 1 and 2) or active (grades 3 and 4). Smoking was classified as either current or non/ex-smoker. No quantitative estimation of smoking was attempted.

We aimed to select about 1200 adults aged 25 years and over who were normally resident in the chosen communities. This number was calculated to offer an 85% chance of detecting a prevalence of diabetes of 5% with a relative 95% CI of plus or minus 20%, assuming an 85% response rate.[12](http://www.thelancet.com/journals/lancet/article/PIIS0140-6736%2805%2967662-3/fulltext%22%20%5Cl%20%22bib12%22%20%5Co%20%22) In each community, households were used as the primary sampling unit, a household being judged to accommodate an average of two adults. After being allocated sequential numbers during the pre-survey census, the households were chosen by random number selection in each village, the proportion of households selected varying according to the size of the community. All individuals in each selected household who fulfilled the criteria for study enrolment were invited to participate.

**Statistical analysis**

We analysed data with Stata statistical software (Release 8.0, 2003. Stata Corporation, College Station, TX, USA). In addition to crude prevalence estimates, data were examined by 10-year age groups, and age-standardised estimates were calculated using a standard world population conforming to that used for the global prevalence estimates compiled by WHO.[13](http://www.thelancet.com/journals/lancet/article/PIIS0140-6736%2805%2967662-3/fulltext#bib13) Univariate comparisons were undertaken by means of 95% confidence intervals or Student's *t* test for means, and the χ2 test for proportions. Multiple logistic regression was used to examine the independent contribution of individual factors to the total variance in blood glucose values. To make allowance for multiple comparisons, we used the conservative value of p<0·01 as a test of significance. Trends by age were tested by a Wilcoxon-type test for trend with Stata. Numerical estimates for the number of people with diabetes in Cambodia in 2004 were calculated using DISMOD II software[14](http://www.thelancet.com/journals/lancet/article/PIIS0140-6736%2805%2967662-3/fulltext%22%20%5Cl%20%22bib14%22%20%5Co%20%22) in accord with the latest WHO reports.[15](http://www.thelancet.com/journals/lancet/article/PIIS0140-6736%2805%2967662-3/fulltext#bib15), [16](http://www.thelancet.com/journals/lancet/article/PIIS0140-6736%2805%2967662-3/fulltext%22%20%5Cl%20%22bib16)

**Role of the funding source**

The sponsor of the study had no role in study design, data collection, data analysis, data interpretation, or writing of the report. The corresponding author had full access to all the data in the study and had final responsibility for the decision to submit for publication.

**Results**

At Siemreap, the response rate was 100% and 1051 individuals were examined (150 were absent from their village at the time of the survey, which is not unusual in rural areas). At Kampong Cham, the response rate was 91% and 1195 individuals were examined. These high response rates were attained by the active involvement of local medical authorities and local leaders.

The age structure of the two survey populations, and that of the 2004 Cambodian Inter-Censal Survey,[5](http://www.thelancet.com/journals/lancet/article/PIIS0140-6736%2805%2967662-3/fulltext%22%20%5Cl%20%22bib5%22%20%5Co%20%22) is shown in [table 1](http://www.thelancet.com/journals/lancet/article/PIIS0140-6736%2805%2967662-3/fulltext%22%20%5Cl%20%22tbl1%22%20%5Co%20%22). At all ages, women outnumbered men in both surveys. This finding is almost universal in developing countries, since men are more likely than women to be absent because of their wage-earning activities.



**Table 1**[**Table image**](http://www.thelancet.com/journals/lancet/article/PIIS0140673605676623/table?tableid=tbl1&tableidtype=table_id&sectionType=red)

Age and sex structure of two survey samples and population of Cambodia aged 25 years and older

The prevalence of diabetes and impaired glucose tolerance is shown in [table 2](http://www.thelancet.com/journals/lancet/article/PIIS0140-6736%2805%2967662-3/fulltext%22%20%5Cl%20%22tbl2%22%20%5Co%20%22). Overall prevalence of diabetes was 5% at Siemreap and 11% at Kampong Cham. Prevalence of impaired glucose tolerance was 10% at Siemreap and 15% at Kampong Cham. Thus, total prevalence of abnormal glucose tolerance was 15% at Siemreap and 26% at Kampong Cham. Apart from a modest excess of impaired glucose tolerance in women at Kampong Cham, prevalence of abnormal glucose tolerance was similar in men and women. Prevalence of diabetes and impaired glucose tolerance rose with age. A decline in prevalence of diabetes at older ages was recorded at Siemreap, but prevalence rose throughout the age range at Kampong Cham. In almost all age and sex strata, prevalence of impaired glucose tolerance exceeded that of established diabetes, especially at Siemreap, where diabetes was virtually absent in people younger than 35 years.



**Table 2**[**Table image**](http://www.thelancet.com/journals/lancet/article/PIIS0140673605676623/table?tableid=tbl2&tableidtype=table_id&sectionType=red)

Number of participants, prevalence of diabetes, number of newly diagnosed cases, and prevalence of impaired glucose tolerance (IGT), by age (years)

Overall, two-thirds of all people with diabetes were unaware of their condition. Undiagnosed diabetes was more frequent at Siemreap than at Kampong Cham. Undiagnosed diabetes was slightly more common in men than in women. Most patients with diagnosed diabetes were treated with oral hypoglycaemic drugs (11 [69%] at Siemreap and 45 [82%] at Kampong Cham). Very few people with known diabetes were treated with insulin (none at Siemreap and three [5%] at Kampong Cham) or diet alone (<5% in each case). Herbal medications were taken by six (38%) diabetic people at Siemreap and eight (15%) at Kampong Cham, in most cases as an adjunct to oral hypoglycaemic therapy. More than half of the people diagnosed with hypertension were unaware of their condition. At Siemreap, ten (20%) people with known hypertension received medication, and at Kampong Cham the corresponding number was 83 (58%).

Further information on the factors of interest in the survey are summarised in [tables 3](http://www.thelancet.com/journals/lancet/article/PIIS0140-6736%2805%2967662-3/fulltext%22%20%5Cl%20%22tbl3%22%20%5Co%20%22) and [4](http://www.thelancet.com/journals/lancet/article/PIIS0140-6736%2805%2967662-3/fulltext%22%20%5Cl%20%22tbl4%22%20%5Co%20%22). Mean age was higher in Kampong Cham than in Siemreap (p<0·00001). Mean age was similar in men and women (p=0·81). Participants with abnormal glucose tolerance were older than those with normal glucose tolerance (p<0·0001). 139 (13%) participants at Siemreap and 274 (23%) at Kampong Cham were classified as overweight (p<0·0001). There was a stepwise increase in BMI, waist-hip ratio, and overweight between normal, impaired glucose tolerant, and diabetic people (p=0·0017).



**Table 3**[**Table image**](http://www.thelancet.com/journals/lancet/article/PIIS0140673605676623/table?tableid=tbl3&tableidtype=table_id&sectionType=red)

Clinical and anthropometric characteristics of participants in relation to glucose tolerance, Siemreap



**Table 4**[**Table image**](http://www.thelancet.com/journals/lancet/article/PIIS0140673605676623/table?tableid=tbl4&tableidtype=table_id&sectionType=red)

Clinical and anthropometric characteristics of participants in relation to glucose tolerance, Kampong Cham

123 (12%) participants at Siemreap and 299 (25%) at Kampong Cham were classified as hypertensive (p<0·0001). Both systolic and diastolic mean blood pressures showed an increasing trend across levels of glucose tolerance. This relation was observed in men and women in both Siemreap and Kampong Cham (p<0·0001 for trend). At Siemreap, 301 (80%) men and 417 (62%) women were classified as habitually physically active. At Kampong Cham the corresponding numbers were significantly lower; 259 (59%) for men (p<0·0001) and 351 (47%) for women (p<0·0001). Cigarette smoking was more common at Siemreap than at Kampong Cham (p<0·0001), and more common in men than women (p<0·0001). There was no obvious relation between smoking habit and level of glucose tolerance.

Trends for mean blood glucose concentration, blood pressure, BMI, and waist-hip ratio across age groups are shown in [table 5](http://www.thelancet.com/journals/lancet/article/PIIS0140-6736%2805%2967662-3/fulltext%22%20%5Cl%20%22tbl5%22%20%5Co%20%22). The trends were mostly highly significant within groups and were generally higher for Kampong Cham at the 95% significance level.



**Table 5**[**Table image**](http://www.thelancet.com/journals/lancet/article/PIIS0140673605676623/table?tableid=tbl5&tableidtype=table_id&sectionType=red)

Relation between age and blood glucose, BMI, waist-hip ratio, and blood pressure

The questionnaire completed by all participants included questions relating to dietary habits. In all villages, daily consumption of fruit and vegetables was the norm. Highest consumption of fish was at Siemreap. Meat consumption was more variable, though generally more common at Kampong Cham (data not shown).

To assess the independent effect of the principal factors on glucose tolerance, as indicated by the 2-h blood glucose concentration, linear regression models were explored ([table 6](http://www.thelancet.com/journals/lancet/article/PIIS0140-6736%2805%2967662-3/fulltext%22%20%5Cl%20%22tbl6%22%20%5Co%20%22)). Female sex, older age, waist-hip ratio, SBP, and DBP were significant predictors of individuals' blood glucose concentration. However, as is often the case, the model explained only a minority (10%) of total variance.



**Table 6**[**Table image**](http://www.thelancet.com/journals/lancet/article/PIIS0140673605676623/table?tableid=tbl6&tableidtype=table_id&sectionType=red)

Multiple linear regression

The association between glucose intolerance, obesity, and hypertension is well documented in many populations.[17](http://www.thelancet.com/journals/lancet/article/PIIS0140-6736%2805%2967662-3/fulltext%22%20%5Cl%20%22bib17%22%20%5Co%20%22) Co-morbidity between glucose intolerance (diabetes plus impaired glucose tolerance), central obesity (indicated by waist-hip ratio), and hypertension is shown in the [figure](http://www.thelancet.com/journals/lancet/article/PIIS0140-6736%2805%2967662-3/fulltext%22%20%5Cl%20%22fig1%22%20%5Co%20%22). About a third of participants at Siemreap and half of those at Kampong Cham had one or more of these conditions. Isolated glucose intolerance was more common at Siemreap, whereas isolated central obesity was found most frequently at Kampong Cham. Co-morbidity (two or more conditions in the same person) was seen in only 9% (95) of individuals at Siemreap, but in 25% (299) at Kampong Cham, where 7% (84) of people had all three conditions.

**Figure** [**Full-size image**](http://www.thelancet.com/journals/lancet/article/PIIS0140673605676623/images?imageId=gr1&sectionType=red) **(49K)** [**Download to PowerPoint**](http://download.thelancet.com/ppt/journals/0140-6736/PIIS0140673605676623.ppt?id=e16241398b8eb460:71561c3c:12b65c2fb1f:2fb01285908888467&ll=gr1)

Prevalence of comorbidity

**Discussion**

The most important finding from these two surveys is that diabetes is considerably more frequent in Cambodia than was previously expected. The study provides surprising information on the burden of diabetes in a region hitherto little studied, and this information is now leading to a re-consideration of health policy and priorities at a national level.

With a very large population and rapid economic growth, Asia is considered as the epicentre of the modern diabetes pandemic. India and China are estimated to have the largest numbers of people with the disease.[15](http://www.thelancet.com/journals/lancet/article/PIIS0140-6736%2805%2967662-3/fulltext#bib15) However, since the countries of Indochina have only recently emerged from poverty and relative political isolation, they have been thought to be at less risk. Recent survey data from Vietnam tended to support this notion (Khai PG, Vietnam Heart Institute, Hanoi, Vietnam. Personal communication), but our results from Cambodia tell another story. The prevalence of glucose intolerance in the traditional rural villages near Siemreap was as high as in Hanoi (the capital city of Vietnam) and in a recent multicentre study in Thailand,[18](http://www.thelancet.com/journals/lancet/article/PIIS0140-6736%2805%2967662-3/fulltext#bib18) a country with a long-established market economy. Prevalence of glucose intolerance at Kampong Cham (more than a quarter of all adults examined) probably ranks as the highest recorded in the region to date. The higher prevalence of comorbidity at Kampong Cham than in Siemreap is also notable.

Our surveys used universal glucose tolerance testing, as did the study in Vietnam. The study in Thailand used fasting blood-glucose estimation, but the two methods are similar, with the difference between estimates using the different methods being positive in some and negative in other populations.[19](http://www.thelancet.com/journals/lancet/article/PIIS0140-6736%2805%2967662-3/fulltext#bib19), [20](http://www.thelancet.com/journals/lancet/article/PIIS0140-6736%2805%2967662-3/fulltext%22%20%5Cl%20%22bib20) Although response rate was good in both surveys, the unequal number of men and women available for study was unfortunate. It could be assumed that men absent from their home by reason of employment would not be seriously ill. If all absent men were free of diabetes (the most extreme assumption), the prevalence of the condition in men could have been underestimated. However, the prevalence of diabetes was found to be similar in men and women in both Siemnreap and Kampong Cham, suggesting that this bias did not seriously affect the results.

The people of Cambodia are not obese by international standards, and glucose intolerance was found to be common at Siemreap, where people are almost uniformly lean. Therefore, other explanations must be sought for the high prevalence of glucose intolerance in a country that is classified among the world's least developed nations. Two possible theories deserve further investigation. First, Cambodians were exposed to strong cultural and genetic effects from India in their early history, and the population of the Indian subcontinent is known to be very susceptible to diabetes.[18](http://www.thelancet.com/journals/lancet/article/PIIS0140-6736%2805%2967662-3/fulltext%22%20%5Cl%20%22bib18%22%20%5Co%20%22) Therefore, Cambodia could have inherited a greater susceptibility to glucose intolerance than other countries in Indochina. Secondly, an association between diabetes in later life and nutritional deprivation in fetal life and infancy has been proposed.[19](http://www.thelancet.com/journals/lancet/article/PIIS0140-6736%2805%2967662-3/fulltext%22%20%5Cl%20%22bib19%22%20%5Co%20%22) The hardship of the Cambodian people during the second half of the 20th century, particularly under the rule of the Khmer Rouge (1975—79), may have left a grim legacy. Cohort analysis of patients born during the Khmer Rouge era could be of interest in putting this so-called thrifty phenotype hypothesis to the test.

Two-thirds of all cases of diabetes were undiagnosed before the survey. This finding is similar to those in other studies in developing regions of the world (the global average is around 50%),[13](http://www.thelancet.com/journals/lancet/article/PIIS0140-6736%2805%2967662-3/fulltext#bib13) and highlights the need for greater public awareness, professional education, and strengthening of diabetes-related health services.

The prevalence estimates we present translate to a total of 255 000 people with diabetes in Cambodia. This number contrasts sharply with the latest estimate from WHO of 110 000, which was based on an assumed national prevalence of 1·9% in adults aged 20 years and older.[15](http://www.thelancet.com/journals/lancet/article/PIIS0140-6736%2805%2967662-3/fulltext#bib15) To appreciate the full effect of noncommunicable diseases to the Cambodian population, the additional burden of impaired glucose tolerance and hypertension must also be added. The results of these surveys might also have wider implications. Despite the fact that estimates of the frequency of diabetes worldwide[13](http://www.thelancet.com/journals/lancet/article/PIIS0140-6736%2805%2967662-3/fulltext%22%20%5Cl%20%22bib13), [15](http://www.thelancet.com/journals/lancet/article/PIIS0140-6736%2805%2967662-3/fulltext%22%20%5Cl%20%22bib15), [23](http://www.thelancet.com/journals/lancet/article/PIIS0140-6736%2805%2967662-3/fulltext%22%20%5Cl%20%22bib23) seem at first to be quite comprehensive, they are based on many extrapolations for countries in which national data are unavailable. If the frequency of diabetes in Cambodia was so underestimated, could we still be failing to recognise a similar situation in other socioeconomically underprivileged populations?

**Contributors**

H King prepared the study protocol, trained the survey team, and coordinated the interpretation of results and preparation of the report. L Keuky contributed to the choice of study populations, coordinated the overall supervision of the project in Cambodia, and liaised with national and international partners. S Seng and T Khun supervised the day-to-day survey work and did on-site data entry. G Roglic analysed the survey data, prepared it for publication, and contributed to its interpretation and presentation in the report. M Pinget took overall responsibility for the project and took the final decision for publication of the results.

**Conflict of interest statement**

We declare that we have no conflict of interest.

**Acknowledgments**

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