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OBESITY AND DIABETES

Is there a divergence in time trends in the prevalence of impaired glucose tolerance and diabetes? A systematic review in South Asian populations

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Objective Recently, diabetes prevalence has increased in South Asians making it a global public health priority. There are suggestions that pre-diabetes, including impaired glucose tolerance (IGT), may not be increasing. We conducted a systematic review to explore the paradox.

Research Design and Methods We searched electronic databases from inception to June 2009 for cross-sectional studies providing prevalence of pre-diabetes (using WHO criteria) in South Asian adult populations. Two reviewers independently screened articles, performed data extraction, quality appraisal and study classification with any discrepancies resolved by consensus. Repeated cross-sectional studies, categorized by pre-specified criteria, were used for the primary analysis, supplemented by analysis of comparable and all studies.

Results In total, 79 cross-sectional data sets (from 69 published studies) were identified resulting in the inclusion of 179 408 people. Four sets of repeated cross-sectional studies, conducted in Chennai, rural Tamil Nadu, Mauritius and Singapore ($n = 30\,399$), provided time trend information. Three of them showed an increase in diabetes prevalence ($P < 0.001$) whereas IGT fell in two ($P < 0.05$), and was stable in the remainder. A similar pattern was seen among three other sets of comparable studies ($n = 58\,820$) and in scatterplots of all 79 data sets.

Conclusion This novel systematic review is the first to assess secular trends of pre-diabetes in any population. The data show diabetes prevalence is rising, whereas IGT prevalence is stable or falling. Explanations include: recent environmental or lifestyle changes favouring an increased rate of conversion from IGT to diabetes, or a cohort effect with improving maternal and infant nutrition resulting in reduced IGT with a fall in diabetes to follow.

Keywords Diabetes mellitus, epidemiology, prevalence, systematic review

Table 1 The major diagnostic criteria for DM, IGT and IFG based on venous plasma measurements

Diagnostic criteria and references	Diabetes	Borderline DM/IGT	IFG
WHO 1965[41]	FPG >7.2 mmol/l	Borderline diabetes: FPG 6.0–7.2 mmol/l	
WHO 1980[42]	FPG ⩾7.8 mmol/l or 2-h gluc ⩾11.1 mmol/l	FPG <7.8 mmol/l and 2-h gluc ⩾7.8 mmol/l and <11.1 mmol/l	
WHO 1985[43]			
ADA 1997[44]	FPG ⩾7 mmol/l		FPG 6.1–6.9 mmol/l
WHO 1998[45]	FPG ⩾7 mmol/l or 2-h gluc ⩾11.1 mmol/l	FPG <7 mmol/l and 2-h gluc ⩾7.8 mmol/l and <11.1 mmol/l	FPG 6.1–6.9 mmol/l and 2-h gluc <7.8 mmol/l if measured
WHO 2006[46]			
ADA 2004[32]	FPG ⩾7 mmol/l		FPG 5.6–6.9 mmol/l

FPG, fasting plasma glucose; 2-h gluc, 2-h glucose; DM, diabetes mellitus; IGT, impaired glucose tolerance; IFG, impaired fasting glucose.

Introduction

Diabetes mellitus (DM) is an important public health problem, affecting an estimated 285 million adults in 2010, and predictably increasing to 439 million adults by 2030.[1] South Asians, in particular, are at an increased risk of diabetes compared with European origin White populations with India, predicted to have 87 million people living with diabetes by the year 2020, the greatest burden within any country.[1–3]

Impaired fasting glucose (IFG) and impaired glucose tolerance (IGT) are states of pre-diabetes that not only pre-dispose to diabetes but are themselves associated with an increased risk of many diabetic complications, including cardiovascular disease and death.[4–6] Both the World Health Organization (WHO) and the American Diabetes Association (ADA) have created standardized diagnostic criteria for IFG, IGT and DM, which have been revised over time (summarized in Table 1). Whereas the natural history of pre-diabetes and its progression to type 2 diabetes is unclear, evaluating trends in pre-diabetes prevalence may help in predicting the future of the diabetes epidemic by understanding changes in the number of people at increased risk. This may have major implications for understanding the natural history, disease prediction at the population level and health-care planning—both for diabetes and pre-diabetes treatment.

Well-conducted randomized controlled trials have found both lifestyle interventions and medications in those with IGT can prevent progression to diabetes, thus making the case for treatment to be targeted at pre-diabetic individuals.[7,8] The Prevention of Diabetes in South Asians (PODOSA) study is an Edinburgh-based randomized controlled trial, which aims to study the impact of lifestyle interventions on South Asians to prevent diabetes.[9] The expected prevalence of IGT in a selected high-risk group was 30% based on previous assessments carried out in the Newcastle Heart Project in 1995–97 and supported by other existing evidence (R.Bhopal, personal communication).[10] Unexpectedly, a prevalence of only 10.8% was found during study recruitment for PODOSA, raising the possibility that IGT prevalence might be falling.

Other studies have suggested pre-diabetes prevalence may be falling. In 1993, King and Rewers[11] compared the proportion of dysglycaemia due to IGT with the prevalence of diabetes in cross-sectional studies conducted across many populations over different time points. They found a negative correlation: studies with higher diabetes prevalence did not have a proportionate increase in IGT. However, this study only investigated the relative contribution of IGT to dysglycaemia, with no assessment of changes in absolute prevalence over time. More recently, Mohan *et al.*[12] noted the prevalence of IGT was falling, whereas diabetes was increasing in an analysis of repeated cross-sectional studies conducted in Chennai, India.

However, to our knowledge, the relationship between IGT and DM has not been systematically investigated for the same population over time. We, therefore, conducted a systematic review of all published cross-sectional studies reporting on the prevalence of diabetes and pre-diabetes in South Asian populations worldwide.

Methods

Search strategy and selection criteria

We searched electronic databases from inception to June 2009: Medline (Ovid); Embase (Ovid); Global Health (Ovid); and the Science Citation Index Expanded (ISI Web of Science), without language restrictions. Search terms included 'South Asian$', 'Indian$', 'Pakistan$', 'Diabet$', 'Pre-diabet$', 'Impaired glucose tolerance', 'Oral glucose tolerance test', 'Prevalence' and 'Cross-section'. The search strategies were created in conjunction with a medical librarian and the full strategy described in the online supplement. Reference lists of all included studies

Table 2 Reasons for excluding articles based on abstract, full paper and for added article

Reason for exclusion	No. of articles based on abstract	No. of articles based on full paper	No. of added articles excluded	Total no. of articles excluded
No data available for South Asians	2	5	2	9
Paediatric population studied	1	1	0	2
WHO biochemical criteria not used	19	40	4	63
Studied less than 100 participants	2	0	0	2
Appropriate study design for prevalence not used	3	7	0	10
Studied individuals with known diabetic states	0	0	1	1
Studied pregnant individuals only	0	0	0	0
Studied individuals selected on the basis of a state	0	0	0	0
Measured random glucose only	5	10	1	16
Published in a language other than English	0	0	0	0

were scrutinized and citation searches (using Google Scholar) conducted.

All articles were independently screened by two reviewers (S.V.K. and J.R.M.) and discrepancies discussed. Inclusion and exclusion criteria were determined following pilot searches. We included studies that: published data for South Asians (defined here as individuals originating from the Indian subcontinent—Bangladesh, India, Pakistan or Sri Lanka); included an adult population (defined as $\geqslant$16 years of age); used biochemical methods to classify participants as borderline DM/IGT/IFG based on WHO criteria; included at least 100 participants and used a cross-sectional design (or the cross-sectional phase of a cohort study) to determine prevalence.

We excluded articles studying only individuals with known diabetes status, pregnant individuals, populations screened as high risk (e.g. on the basis of body mass index or random blood glucose) or populations sharing specific disease states. Non-English language articles were excluded during the screening process. Repeat publications of the same data set were excluded. Journal articles were chosen in preference over conference abstracts when both presented the same data. The reasons for exclusion are provided in Table 2 and a full list of the excluded articles is available as Supplementary Data at *IJE* online.

Outcomes

The primary outcome was overall prevalence of pre-diabetes (borderline DM, IGT, IFG) based on WHO criteria ascertained using an oral glucose tolerance test and/or a fasting plasma glucose.

Secondary outcomes were sex-specific prevalence of pre-diabetes and overall and sex-specific prevalence of type 2 DM. The DM prevalence included both self-reported and newly detected cases.

Data gathering and quality assessment

Quality criteria based on existing guidelines were developed prior to data extraction.[13–15] These included: descriptions of study setting; study population (including sampling frame, eligibility criteria, demographic details, response rate and characteristics of non-responders); measurement methods and the use of appropriate statistics. Standardized data extraction forms were used for all short-listed studies by both reviewers. Authors of included studies were contacted on a maximum of two occasions to obtain year of fieldwork if not available in published reports.

Analysis and statistics

Three stages of analyses were undertaken independently by both reviewers. Disagreements were resolved by consensus and contacting authors of the original studies when appropriate.

Stage 1: repeated cross-sectional studies

Studies were characterized and identified as repeated cross-sectional studies if they studied the same (i) geographical area; (ii) age and sex population structure; and (iii) urbanization category (urban, semi-urban, rural, national).

Stage 2: comparable studies

Studies were characterized and identified as comparable if they studied the same (i) country; (ii) age and sex population structure; (iii) urbanization category (urban, semi-urban, rural, national); and (iv) used a general population. Studies that had been used in the first stage of analysis were used again in the second stage if relevant.

Stage 3: all remaining studies

Prevalence data were extracted for all included studies and plotted against time.

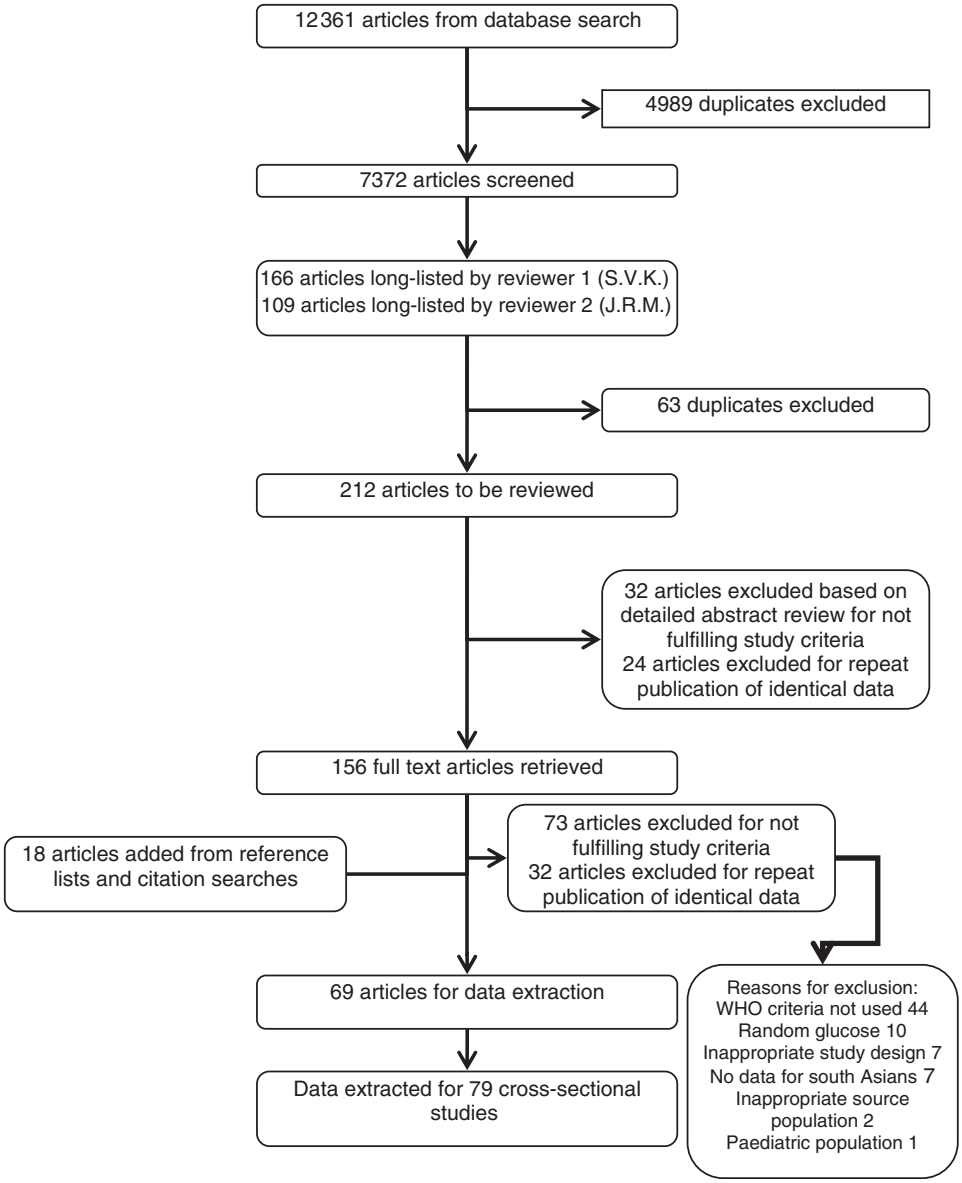

Figure 1 Flow diagram of search strategy and study selection

Age-standardized prevalences were extracted in preference to crude prevalences, with studies using the same reference population used whenever available. For repeated cross-sectional studies, authors were contacted to provide age-standardized prevalences using the same reference population. Sex standardization was undertaken, assuming an equal weighting of males and females for all studies providing sex-specific prevalence rates.

All data were analysed using SPSS v17.0 (SPSS Inc., IL, USA). Trends of prevalence across time for repeated cross-sectional studies were tested using chi-square tests for trend with one degree of freedom. Analyses were undertaken for urban, semi-urban and rural regions separately.

Results

In total, 12 361 articles were identified by electronic database searches with 7372 articles screened following de-duplication. A total of 69 articles relating to 79 cross-sectional data sets were identified (see Figure 1 for search strategy) resulting in the inclusion of 179 408 people. Detailed information on included studies is available as Supplementary Data at *IJE* online. Six data sets of repeated cross-sectional studies were identified for the first stage of the analysis (Table 3). A further six data sets of comparable studies, involving similar populations, were selected for the second stage of the analysis (Table 3).

Table 3 Summary of included studies

Place	Study year	References	Number studied	Age in years, mean (SD)	Sex (% male)	Response rate (%)	Diagnostic criteria	Measurement method	Standard population
Summary of repeated studies									
Chennai, India	1988	Ramachandran *et al.*[17]	900	38 (12)	51	91	WHO 1985	Capillary	1991 Chennai
	1994	Ramachandran *et al.*[19]	2183	40 (12)	51	84	WHO 1985	Venous	1991 Chennai
	1996	Mohan *et al.*[20]	1262	42.8[a]	44[a]	90	WHO 1999	Venous	1991 Chennai
	2000	Ramachandran *et al.*[18]	1668	44 (15)	42	90	WHO 1985	Capillary	1991 Chennai
	2003	Mohan *et al.*[12]	2350	NR	NR	90	WHO 1998	Venous	1991 Chennai
	2006	Ramachandran *et al.*[16]	2192	38	48	82	WHO 1998	Venous	1991 Chennai[b]
Mauritius	1987	Soderberg *et al.*[23]	3254	42[a]	48	86	WHO 1998	Venous	1992 Mauritius
	1992	Soderberg *et al.*[23]	4327	45.6[a]	47	90	WHO 1998	Venous	1992 Mauritius
	1998	Soderberg *et al.*[23]	3747	48.8[a]	45	87	WHO 1998	Venous	1992 Mauritius
Rural Tamil Nadu, India	1989	Ramachandran *et al.*[17]	1038	41 (15)	50	88	WHO 1998	Capillary	1991 rural TN
	1997	Ramachandran *et al.*[22]	1637	36[a]	46	88	WHO 1985	Capillary	1991 rural TN
	2003	Ramachandran *et al.*[21]	1213	41 (6)	41	75	WHO 1998	Capillary	1991 rural TN
	2006	Ramachandran *et al.*[16]	2584	38	50	87	WHO 1998	Venous	1991 rural TN[b]
Singapore	1992	Tan *et al.*[26]	586	NR	51	73	WHO 1985	Venous	2000 Singapore[b]
	1998	Ministry of Health[25]	850	NR	46	65	WHO 1985	Venous	2000 Singapore[b]
	2004	Bhalla *et al.*[24]	608	NR	47	57	WHO 1985	Venous	2000 Singapore[b]
Dhaka, Bangladesh	1996	Abu Sayeed *et al.*[30]	1052				WHO 1985	Capillary	1991 census (age 30–64 years)
	2002	Sayeed *et al.*[31]	4157				WHO 1998	Venous	2000 census (age 30–70 years)
Sri Lanka	1990	Illangasekara *et al.*[28]	1999	NR	40	99	WHO 1985	Venous	Not performed
	2000	Illangasekara *et al.*[29]	200	NR	47	91	WHO 1998	Venous	Not performed
Summary of comparable studies									
Urban India	1988	Ramachandran *et al.*[17]	900	38 (12)	51	91	WHO 1985	Capillary	1991 Chennai
	1993	Singh *et al.*[47]	158	40[a]	53	NR	WHO 1980	Unknown	Not performed
	1994	Ramachandran *et al.*[19]	2183	40 (12)	51	84	WHO 1985	Venous	1991 Chennai
	1996	Mohan *et al.*[20]	1262	42.8[a]	44[a]	90	WHO 1999	Venous	1991 Chennai
	1999	Iyer *et al.*[48]	520	49[a]	NR	72	WHO 1985	Venous	Not performed
	1999	Zargar *et al.*[49]	1038	50 (8)	49	94%	WHO 1998	Capillary	Not performed
	1999	Kutty *et al.*[50]	224	NR	42	70	WHO 1998	Venous	1996 WHO (age 30–64 years)
	2000	Sadikot *et al.*[51]	10 617	NR	51	80	WHO 1998	Capillary	1991 India
	2000	Gupta *et al.*[52]	1091	NR	49	61	WHO 1998	Unknown	1991 Jaipur
	2000	Ramachandran *et al.*[18]	1668	44 (15)	42	90	WHO 1985	Capillary	1991 Chennai

(continued)

Table 3 Continued

Place	Study year	References	Number studied	Age in years, mean (SD)	Sex (% male)	Response rate (%)	Diagnostic criteria	Measurement method	Standard population
	2003	Menon *et al.*[53]	986	44.8[a]	40	32	WHO 1998	Capillary	Not performed
	2003	Mohan *et al.*[20]	2350	NR	NR	90	WHO 1998	Venous	1991 Chennai
	2006	Ramachandran *et al.*[16]	2192	38	48	82	WHO 1998	Venous	1991 Chennai
	2008	Das *et al.*[54]	193	NR	54	90	WHO 1998	Venous	Unknown
Semi-urban India	2006	Deo *et al.*[55]	1022	42[a]	46	98	WHO 1998	Unknown	Unknown
	2006	Ramachandran *et al.*[16]	2290	37	43	88	WHO 1998	Venous	2001 TN
Rural India	1989	Ramachandran *et al.*[17]	1038	41 (15)	50	88	WHO 1998	Capillary	1991 rural TN
	1990	Patandin *et al.*[56]	467	54	41	95	WHO 1985	Capillary	Not performed
	1993	Singh *et al.*[47]	168	40[a]	53	NR	WHO 1980	Unknown	Not performed
	1997	Ramachandran *et al.*[22]	1637	36[a]	46	88	WHO 1985	Capillary	1991 rural TN
	1999	Zargar *et al.*[49]	4045	50 (8)	49	94	WHO 1998	Capillary	Not performed
	1999	Patel *et al.*[57]	285	49[a]	47	63	WHO 1998	Venous	Not performed
	2000	Sadikot *et al.*[51]	7746	NR	47	91	WHO 1998	Capillary	1991 India
	2003	Ramachandran *et al.*[21]	1213	41 (6)	41	75	WHO 1998	Capillary	1991 rural TN
	2006	Ramachandran *et al.*[16]	2584	38	50	87	WHO 1998	Venous	1991 rural TN
	2008	Das *et al.*[54]	157	NR	51	80	WHO 1998	Venous	Unknown
Urban Bangladesh	1996	Abu Sayeed *et al.*[30]	1052	NR	65	NR	WHO 1985	Capillary	1991 census (age 30–64 years)
	2002	Abu Sayeed *et al.*[31]	4157	37 (13)	41	83	WHO 1999	Venous	2000 census (age 30–70 years)
Semi-urban Bangladesh	1996	Abu Sayeed *et al.*[30]	6847	40[a]	65	80	WHO 1980	Capillary	1991 census (age 30–64 years)
	2004	Rahim *et al.*[58]	3981	37	40	80			
Rural Bangladesh	1995	Abu Sayeed *et al.*[59]	1005	NR	45	70	WHO 1985	Capillary	Adjusted to age 30–64 years
	1996	Abu Sayeed *et al.*[30]	1319	NR	60	NR	WHO 1985	Capillary	1991 census (age 30–64 years)
	1999	Abu Sayeed *et al.*[60]	4923	38[a]	47	86	WHO 1999; FPG only	Venous	1991 census data adjusted in 2000
	1999	Hussain *et al.*[61]	4757	NR	42	95	WHO 1998; FPG only	Capillary	WHO's New World Population
	2002	Abu Sayeed *et al.*[62]	1119	NR	42	76	WHO 1998; FPG only	Venous	1996 census
	2004	Rahman *et al.*[63]	975	39[a]	37	98	WHO 1998	Capillary	Not performed

[a]Weighted mean.
[b]Standardized data using the same reference population as other studies obtained from the authors.
NR, Not reported; TN, Tamil Nadu.

Quality

Overall, the quality of the included studies was highly variable. Those included in the repeated and comparable analyses tended to be of higher quality than the remainder. Particular areas of strength included detailed descriptions of sampling methods, high response rates and detailed biochemical methodology. Universal weaknesses included omission of fieldwork dates, lack of description of non-responders and few power calculations. Repeated cross-sectional studies tended to be of high quality with Chennai, rural Tamil Nadu and Mauritius studies being most robust. Analysis of only these studies did not change our findings. Full details of the quality assessments are available as Supplementary Data at *IJE* online.

Repeated cross-sectional studies

Of the six sets of repeated cross-sectional studies identified, four (conducted in Chennai, rural Tamil Nadu, Mauritius and Singapore) provided time trend information.

Six studies were undertaken in Chennai (urban, South India) between 1989 and 2006.[12,16–20] Overall, these studies were performed to a high quality, achieving most of the quality criteria, and studied similar populations (Table 3). Sample sizes varied between 900 and over 2000.

The trends for DM and IGT in Chennai are shown in Figure 2a. Only one study reported the prevalence of IFG, so no trend analysis could be undertaken.[16] A clear increase over time can be seen in the prevalence of DM, from 8.0% to 19.0%, ($P < 0.001$) and this is seen for both males and females (available as Supplementary Data at *IJE* online). In contrast, the prevalence of IGT is more variable with no definite trend visible ($P = 0.052$). However, it is noteworthy that the prevalence appears similar in the first and the last studies. The 2000 study appears to estimate a considerably greater prevalence of IGT than other studies. Reasons for this are unclear but the use of 1985 diagnostic criteria may result in a greater proportion of individuals classified with IGT rather than DM in comparison with the 1998 criteria used in adjacent studies on the graph.

Ramachandran *et al.*[16,17,21,22] conducted four cross-sectional studies in rural parts of Tamil Nadu between 1989 and 2006. Figure 2b shows a clearly increasing DM prevalence (2.1–8.9%; $P < 0.001$) and a falling prevalence of IGT (7.5–5.3%; $P = 0.015$) over time. Sex-specific prevalences are available online for three of the four studies and show that the trends for both IGT and DM do not appear to differ by sex.

Three well-conducted national surveys were performed in Mauritius in 1987, 1992 and 1998.[23] The age- and sex-standardized prevalence of dysglycaemic states for South Asians have been reported separately from other populations surveyed using the WHO 1998 criteria for all three studies. Trends in the prevalence of dysglycaemia are shown in Figure 2c. An increasing DM prevalence (13.0–18.6%; $P < 0.001$) and a falling prevalence of IGT (15.8–14.0%; $P = 0.042$) can be seen. The prevalence of IFG shows no clear trend over time.

Three Ministry of Health national surveys were undertaken in Singapore in 1992, 1998 and 2004 with data presented for South Asians.[24–26] A similar study conducted by Hughes *et al.*[27] in 1982–85 was excluded as the oral glucose tolerance test was only performed on those screened as high risk, based on a fasting plasma glucose level of $\geqslant 6$ mmol/l. Figure 2d suggests a possible increase in DM prevalence ($P = 0.407$) with a stable IGT prevalence ($P = 0.853$). However, the relatively small sample sizes and poor response rates make interpretation difficult.

Illangasekara *et al.*[28,29] performed cross-sectional studies in the Central Province of Sri Lanka in 1990 and 2000 as part of the assessment of the Hindagala Community Health Project. The earlier study determined IGT and the latter IFG; therefore, trends in IGT and IFG could not be assessed, but the age-standardized prevalence of DM increased from 2.5% to 8.5% over this period.

Similarly in Dhaka, rural Bangladesh, studies were undertaken in 1996 and 2002 by Abu Sayeed *et al.*[30] and Sayeed *et al.*[31] with only IGT determined in the former and IFG in the latter. The age-standardized prevalence of DM increased from 8.1% to 10.2% over this period.

Comparable cross-sectional studies

Of the six sets of comparable cross-sectional studies identified, three (rural Bangladesh, urban India and rural India) provided time trend information. No formal statistical analyses were performed given the limited comparability of the underlying data.

Figure 3a shows that the prevalence of DM in rural Bangladesh appears to have increased over time, whereas the prevalence of IGT has fallen.

Figure 3b displays the prevalence of DM and IGT in rural India, which suggests that DM has increased over time, with the greatest prevalences occurring most recently. No clear trend is evident for IGT. A similar pattern is seen in urban India in Figure 3c.

In semi-urban Bangladesh, the prevalence of DM increased from 4.5% in 1996 to 6.9% in 2004. Measurement of IGT was performed only in the first and IFG only in the second, preventing any inferences regarding trends for these conditions.

In semi-urban India, two studies were undertaken in 2006 preventing time trend analysis.

For Dhaka, urban Bangladesh, the same two studies were included as reported above.

All cross-sectional studies

A crude analysis of all cross-sectional studies suggests that the prevalence of DM appears to be increasing

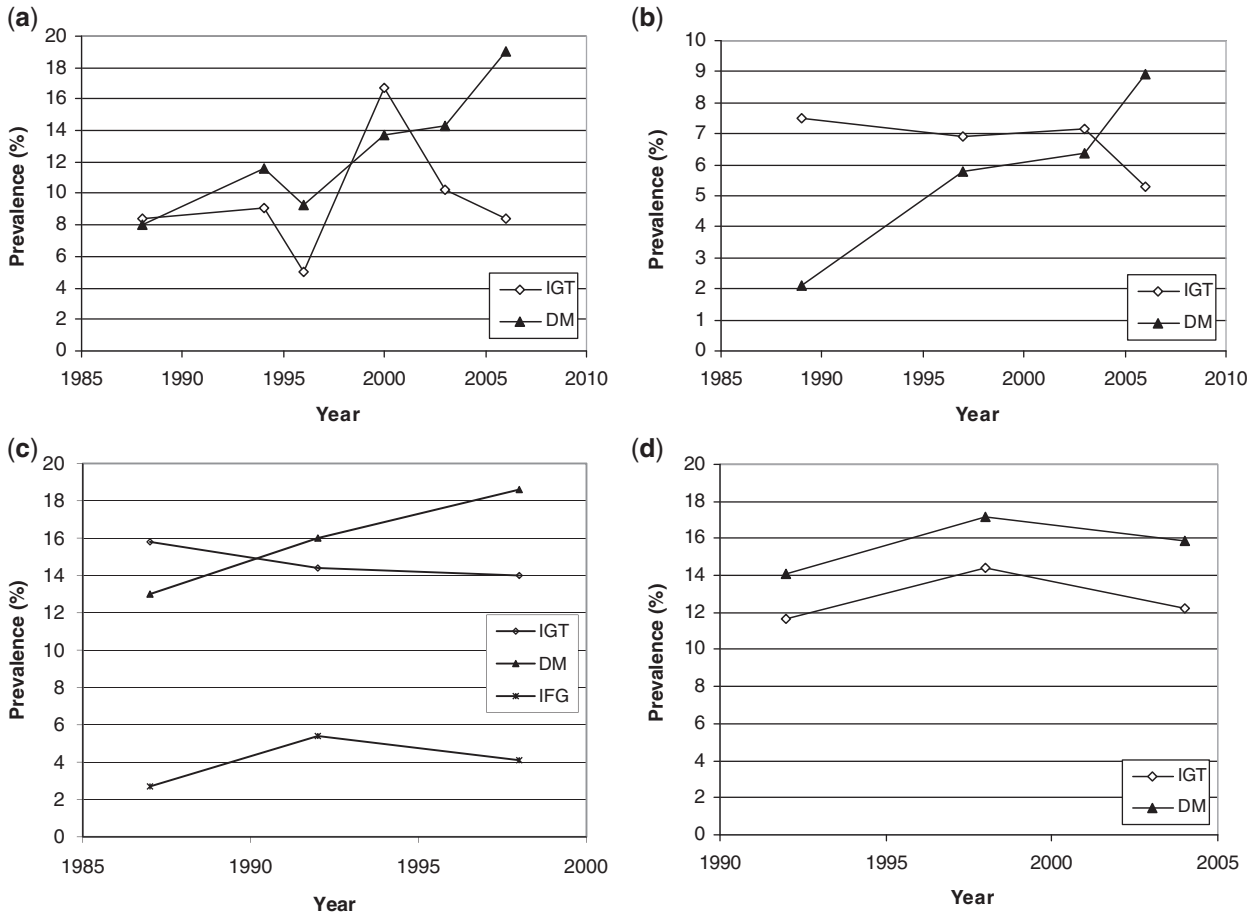

Figure 2 Trends in the prevalence of IGT, IFG and DM in repeated cross-sectional studies. (**a**) Prevalence of IGT and DM in urban India, (**b**) prevalence of IGT and DM in rural India, (**c**) prevalence of IGT, IFG and DM in Mauritius and (**d**) prevalence of IGT and DM in Singapore

with the largest prevalences of DM occurring more recently but the variation in study prevalences is wide (available as Supplementary Data at *IJE* online). In contrast, there appears to be either no change or a decline in IGT prevalence over time.

Discussion

To our knowledge, this is the first systematic review to assess secular trends of pre-diabetes in any population. Our review shows an increasing diabetes prevalence in South Asians, but a stable or falling IGT prevalence. This is surprising given that IGT and DM both share many similar risk factors, which appear to have become more common over time.[32] It was impossible to adequately analyse secular changes in IFG due to a lack of data.

Evaluation of trends in the prevalence of a disease poses a number of methodological problems. Repeated cross-sectional studies are required to determine the changes in the prevalence of a condition.[33] However, there are considerable difficulties in establishing comparability of studies and analysis of studies retrospectively prone to bias. To minimize bias, we have comprehensively searched the literature using pre-specified methodology. A standardized systematic process was followed to identify repeated and comparable studies that could be used to evaluate trends. A three-stage analysis approach was used to identify studies that are as comparable as possible using repeatable criteria. It is inevitable that some differences (including population characteristics, geographical differences and measurement methods) remain between studies but the key finding—divergence in the trend for diabetes and IGT—is unlikely to be an artefact of study methods. Our findings are bolstered by observations on other ethnic groups. For example, in the Mauritius studies, the age-standardized prevalence of diabetes in Creoles rose for the years 1987, 1992 and 1998 from 12.4% to 17.0%, but declined from 16.7% to 13.9% for IGT and from 6.0% to 5.0% for IFG.[23] In addition, a new study has become available during the writing of this article that adds weight to our hypothesis.[34] Anjana *et al.* conducted a large cross-sectional survey of

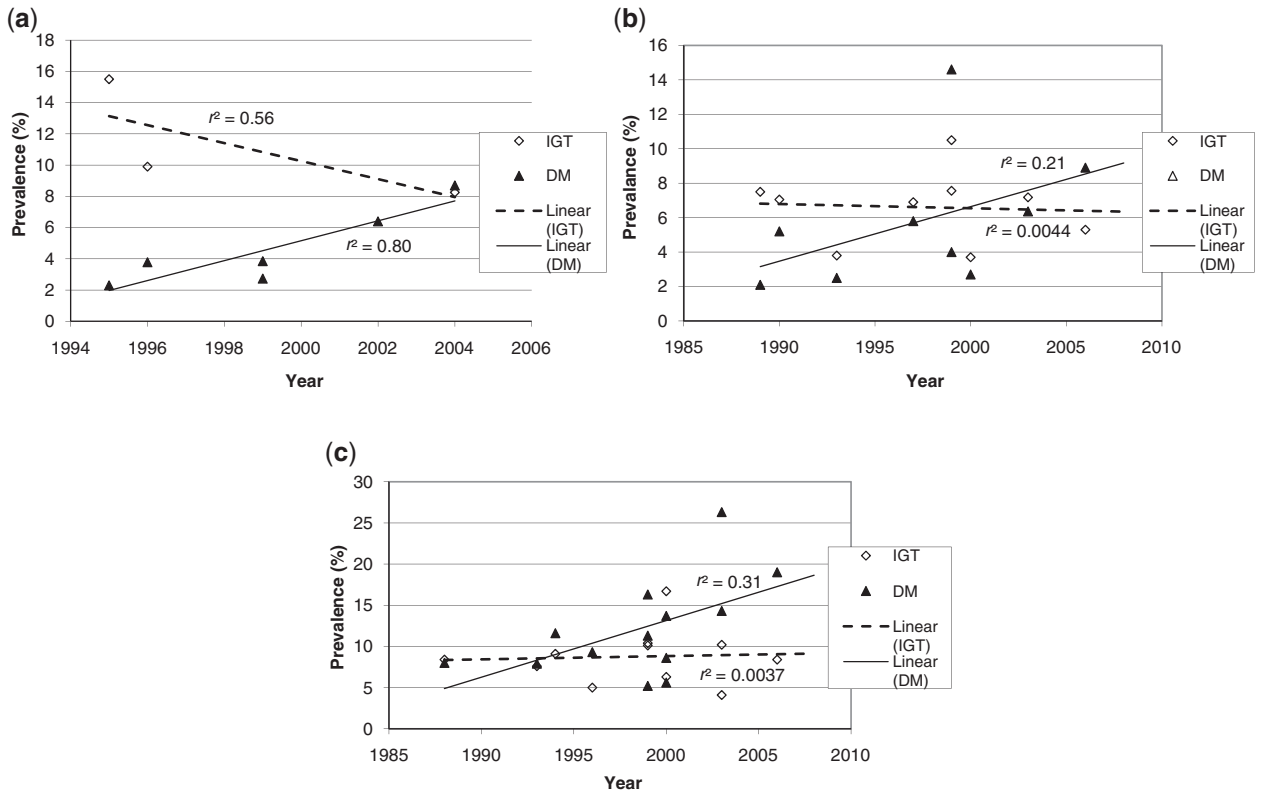

Figure 3 Prevalence of IGT and DM in comparable cross-sectional studies. (**a**) Prevalence of IGT and DM in rural Bangladesh ($n = 6$), (**b**) prevalence of IGT and DM in rural India ($n = 9$) and (**c**) prevalence of IGT and DM in urban India ($n = 13$)

diabetes and pre-diabetes prevalence across four states in India. The prevalence of IGT for rural Tamil Nadu was 2.2% [95% confidence interval (95% CI) 1.6–2.9%], a figure lower than the 5.3% prevalence observed in 2006.

What explanations are there for these trends? The increased availability and reduced expense of testing for diabetes may lead to an increase in those known to have diabetes. The poor replicability of the oral glucose tolerance test could result in individuals who nowadays had been tested for diabetes multiple times as part of their routine care being classified with known diabetes when, with a single test in the past, they would previously have been classified with IGT.[35] However, the Chennai and rural Tamil Nadu studies retested those with known diabetes, making this less likely to happen. Unpublished data from the Diabetes Epidemiology: Collaborative analysis Of Diagnostic criteria in Europe (DECODE) study also suggests that fasting plasma glucose is being more influenced by obesity than 2-h glucose. It is therefore possible that more people may be moving into the diabetes range for this reason.

Mohan *et al.*[12] suggested that the continuing increase in DM with the fall in IGT could occur because conversion from the pool of individuals with IGT to DM is increasing. Alternatively, more rapid progression could occur from the normal state through IGT to DM or potentially skip the IGT state altogether.[12] The former suggests the predictions for the future diabetes epidemic to be overestimates, whereas the latter option suggests the reverse.

The observed changes could also represent a cohort effect. Early life experiences are known to affect the future risk of diabetes with low birthweight babies being at as much as a 3-fold greater risk.[36] Low birthweight and infant malnutrition are common in some Asian populations, with 30% of infants in India estimated to be underweight.[37,38] Improved early life circumstances could therefore lead to future falls in incidence of both diabetes and IGT, but as IGT develops earlier in life, falls in prevalence would be seen first in IGT with later falls occurring in diabetes. Additionally, any falls in diabetes incidence may be masked by the increasing life expectancy of people with diabetes, hence making IGT a more sensitive method to detect such an effect. However, more work will be needed to investigate this possibility as the extent to which maternal malnutrition is responsible for future diabetes in the developing world is yet to be established.

Previous research has found that as DM increases, there is a fall in the proportion of dysglycaemia due to IGT.[39] However, we have demonstrated that this does not appear to merely represent a difference in the proportion of IGT to DM (with IGT not increasing

as much as DM), but that the absolute trends in prevalence appear to differ. Anjana *et al.*'s recent work has interesting implications for our work. They find that the increased prevalence of diabetes in urban compared with rural areas was generally not matched by a proportionate rise in IGT but instead, prevalences within urban areas and within rural areas were similar, raising the possibility of a ceiling effect for IGT.[34] Interestingly, the prevalence of IFG was not consistently higher in urban areas than their rural counterparts, implying IFG prevalence may not increase in line with DM prevalence or remain stable. Our work therefore suggests that the scale of future pre-diabetes might not be as currently expected and has implications for the scale of health service provision for the treatment of pre-diabetes itself.

The natural history of pre-diabetes and its progression to diabetes is unclear. However, this review shows that the pool of individuals with pre-diabetes is reducing—the effect on future diabetes remains to be seen. Further research is needed to explain the apparently contrary trends between prevalence of diabetes and IGT and to investigate if other measures of glycaemic status are undergoing similar changes. This is particularly necessary for HbA1c that is being advocated for diagnostic use.[40] Such research will not only improve our understanding of the population distribution and prediction of diabetes, but also help plan more accurately the future provision of health services.

Supplementary Data

Supplementary Data are available at *IJE* online.

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KEY MESSAGES

- This is the first systematic review to assess secular trends of pre-diabetes in any population.
- This systematic review of prevalence studies in South Asians confirms that diabetes prevalence is increasing but impaired glucose tolerance is either remaining stable or falling.
- A stable or falling prevalence of impaired glucose tolerance over time has major implications for our understanding of disease progression, the future burden of disease and provision of treatment.

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