Global prevalence of prediabetes in children and adolescents: A systematic review and meta-analysis

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Abstract

Background: Prediabetes is a pivotal risk factor for developing diabetes. This meta-analysis was performed to assess the global prevalence of childhood prediabetes.

Methods: A systematic search was conducted for studies of prediabetes prevalence in the general pediatric population from inception until December 2021. Random-effects meta-analysis was used to combine the data. Variations in the prevalence estimates in different subgroups (age group, sex, setting, investigation period, body mass index [BMI] group, family history of diabetes, diagnosis criteria, World Health Organization [WHO] and World Bank [WB] regions) were examined by subgroup meta-analysis.

Results: A total of 48 studies were included in the meta-analysis. The pooled prevalence was 8.84% (95% CI, 6.74%-10.95%) for prediabetes in childhood. Subgroup meta-analyses showed that the prevalence was higher in males than females (8.98% vs 8.74%, P < .01), in older compared to younger children (7.56% vs. 2.51%, P < 0.01), in urban compared to rural areas (6.78% vs. 2.47, P < 0.01), and higher in children with a family history of diabetes than in those without such a history (7.59% vs. 6.80%, P < 0.01). We observed an upward trend in prediabetes prevalence from 0.93% to 10.66% over past decades (P < 0.01). The pooled prevalence increased from 7.64% to 14.27% with increased BMI (P < 0.01). Pooled prevalence was the lowest for criterion A among different diagnosis criteria (P < 0.01). For WHO and WB regions, the European Region and high-income countries yielded the lowest pooled prevalence (P < 0.01).

Conclusions: Elevated prediabetes prevalence in childhood reaches an alarming level. Intensive lifestyle modification is needed to improve the prediabetes epidemic.

Keywords: adolescent, meta-analysis, prediabetes, prevalence, systematic review

Chengyi Han and Qing Song contributed equally to this study.

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Highlights
There was a growing trend in childhood prediabetes prevalence worldwide with time and BMI. Higher prevalence was observed for males than females, older than younger children, urban than rural areas, and children with family histories of diabetes than those without such a history.

1 INTRODUCTION

Diabetes is an important predictor of mortality, morbidity, and health system costs in the world. It is estimated that the number of adults across the globe with diabetes will increase from 432 million (9.3% of the population) in 2019 to 700 million adults (10.9% of the population) by 2045.1 It is not only highly prevalent in adults; the incidence of diabetes has also been increasing among young people.2 In addition, the progress of diabetes in young participants could be faster and more disruptive than in participants with later onset of the disease, causing early morbidity and reduced quality of life.3,4 The early presentation of prediabetes and diabetes in children raises the possibility of an accelerated pathophysiologic process in the young.5

Given that prediabetes has a pivotal role in the risk of developing diabetes6 and that diabetes incidence has increased markedly over recent decades, reliable estimates of the prevalence of prediabetes should serve as the rationale for comprehensive interventions to increase the rate of reversion from prediabetic states to normal glucose tolerance.7,8 Despite a review assessing the prevalence of prediabetes in childhood,9 its prevalence has not been estimated at the global level. This systematic review and meta-analysis therefore synthesizes data on the global prevalence of prediabetes (impaired fasting glucose [IFG], impaired glucose tolerance [IGT], increased glycosylated hemoglobin [HbA1c], or combinations of these) among children and adolescents. The factors potentially associated with childhood prediabetes were also explored to effectively delay and even prevent the development of prediabetes.

2 MATERIALS AND METHODS

2.1 Data source and searches

Focusing on studies published in English up until December 2021, two researchers (C.H. and Q.S.) independently conducted a systematic search of PubMed, Embase, and Web of Science by using a combination of search terms related to prediabetes (Prediabetic State OR Hyperglycemia OR impaired fasting glucose OR impaired glucose tolerance OR pre-diabetes or prediabetes OR borderline diabetes), prevalence (prevalence OR epidemiology), and children (children OR adolescents). We did not obtain gray literature or unpublished research to inform this manuscript. To complement our database, the reference lists of included articles were also searched. Search strategies are outlined in Table S1 in Appendix S1. This study was conducted in accordance with the preferred reporting guidelines for systematic reviews and meta-analyses (PRISMA).

2.2 Study selection

We included (1) studies that reported a community-based children or adolescents (≤20 years of age) population; (2) studies that reported the prevalence of prediabetes (IFG, IGT, or elevated HbA1c) or data to calculate them; (3) cross-sectional studies or cohort studies; and (4) those for which definitions of prediabetes were explicitly provided. We included studies that were conducted with both adults and children where the prevalence data of prediabetes could be disaggregated for the pediatric group. Where multiple articles reported the same investigation, the one giving more complete details or with the largest sample size was included, but when different aspects or subgroups of the same survey were separately reported in different articles, they were selected. We excluded (1) reviews, case reports, editorials, guidelines, or letters to the editor; (2) case-control studies; (3) and surveys that included participants with any disease or complication. If the epidemiological survey lasted more than a year, the year of study completion was used as the time variable. We emailed corresponding authors of the included studies to acquire the years of investigation for the included studies. If the survey time was not obtained after the correspondence, we imputed it by subtracting 4 years from the year of publication based on the mean time difference of the years of investigation and publication for which data are provided in Table S2 in Appendix S1. After removing duplicates articles, the two researchers (C.H. and Q.S.) independently evaluated the retrieved studies to identify those that were relevant. Disagreements were resolved by consensus or by discussion with a third researcher (Y.R.).
2.3 | Data extraction

Information on first author, publishing year, survey time, country, setting (urban versus rural), date source, response rate, age range, sample size, case, crude prevalence rate, and diagnosis criteria was independently extracted by two reviewers (C.H. and Q.S.) for each included study. For cohort studies, we extracted the data for the baseline assessment. The regions of study location were grouped by continent (African Region [AFR], Region of the Americas [AMR], South-East Asia Region [SEAR], European Region [EUR], Eastern Mediterranean Region [EMR], and Western Pacific Region [WPR]) according to World Health Organization (WHO) criteria and income levels (low-income countries: gross national income [GNI] per capita \( \leq \) US$1035; lower-middle-income countries [LMIC]: GNI per capita US$1036-4045; upper-middle-income countries [UMIC]: GNI per capita US$4046-12,535; high-income countries [HIC]: GNI per capita \( \geq \) US$12,536) using the World Bank [WB] data updated in 2019.10

2.4 | Quality assessment

Two reviewers (C.H. and Q.S.) evaluated the quality of the included studies using the 10-item tool developed by Hoy et al11 (Table S3 in Appendix S1). The total score was the sum of scores for each item, with 9 to 10, 6 to 8, and 0 to 5 representing high, moderate, and low quality, respectively. If reviewers’ scores differed, they discussed them until consensus was reached.

2.5 | Statistical analysis

Data are presented as percentages with 95% CI. Heterogeneity of studies was estimated by the Q test and \( I^2 \) index. We used a random-effects model to calculate a pooled estimation of prediabetes prevalence. Subgroup meta-analyses for childhood prediabetes were also conducted to explore the source of heterogeneity of included studies. As a rule, at least three studies had to be available per subgroup. Chi-square and Cochran-Mantel-Haenszel

![Flowchart of study selection](image-url)
TABLE 1 Global prevalence of childhood prediabetes using random-effects meta-analysis and subgroup meta-analysis

| Variable                      | No. of studies | No. of participants | No. of cases | Prevalence (95% CI), % | $I^2, \%$ | $P$ value Q test | Egger test | Begg test | Subgroup difference |
|-------------------------------|----------------|---------------------|--------------|------------------------|---------|------------------|------------|-----------|--------------------|
| Prediabetes                   | 48             | 6 630 296           | 781 596      | 8.84 (6.74–10.95)      | 99.9    | <0.001           | 0.02       | <0.01     | NA                 |
| IFG                           | 36             | 141 927             | 6947         | 6.93 (5.98–7.88)       | 99      | <0.001           | <0.01      | 0.04      | NA                 |
| IGT                           | 7              | 14 265              | 230          | 2.59 (1.00–4.17)       | 96.7    | <0.001           | NA         | NA        | NA                 |
| Elevated HbA1c                | 8              | 55 554              | 8145         | 9.88 (3.81–15.96)      | 99.9    | <0.001           | NA         | NA        | NA                 |

| Gender                        |                |                     |              |                        |         |                  |            |           |                    |
|-------------------------------|----------------|---------------------|--------------|------------------------|---------|------------------|------------|-----------|--------------------|
| Overall                       | 61             | 143 921             | 14 423       | 8.81 (7.61–10.01)      | 99.6    | <0.001           | <0.01      | 0.07      | <0.01             |
| Male                          | 30             | 68 645              | 7446         | 8.98 (6.96–11.01)      | 99.6    | <0.001           | <0.01      | 0.33      |                    |
| Female                        | 31             | 75 276              | 6977         | 8.74 (7.07–10.40)      | 995     | <0.001           | <0.01      | 0.12      |                    |

| Age group, y                  |                |                     |              |                        |         |                  |            |           |                    |
|-------------------------------|----------------|---------------------|--------------|------------------------|---------|------------------|------------|-----------|--------------------|
| Overall                       | 40             | 6 582 579           | 778 353      | 6.87 (4.71–9.03)       | 99.9    | <0.001           | 0.08       | <0.01     | <0.01             |
| 0–9                           | 7              | 11 497              | 230          | 2.51 (1.61–3.41)       | 86.7    | <0.001           | NA         | NA        | NA                 |
| 10–20                         | 33             | 6 571 082           | 778 123      | 7.56 (5.40–10.12)      | 99.9    | <0.001           | 0.01       | <0.01     |                    |

| Setting                       |                |                     |              |                        |         |                  |            |           |                    |
|-------------------------------|----------------|---------------------|--------------|------------------------|---------|------------------|------------|-----------|--------------------|
| Overall                       | 13             | 47 246              | 1687         | 4.76 (3.59–5.93)       | 98.6    | <0.001           | 0.04       | 0.03      | <0.01             |
| Urban                         | 8              | 31 017              | 1214         | 6.78 (4.94–8.61)       | 98.9    | <0.001           | NA         | NA        | NA                 |
| Rural                         | 5              | 16 229              | 473          | 2.47 (0.93–4.02)       | 98      | <0.001           | NA         | NA        | NA                 |

| Investigation period          |                |                     |              |                        |         |                  |            |           |                    |
|-------------------------------|----------------|---------------------|--------------|------------------------|---------|------------------|------------|-----------|--------------------|
| Overall                       | 48             | 6 630 296           | 781 596      | 8.84 (6.74–10.95)      | 99.9    | <0.001           | 0.02       | <0.01     | <0.01             |
| 1993–2000                     | 7              | 18 968              | 126          | 0.93 (0.53–1.32)       | 89.2    | <0.001           | NA         | NA        | NA                 |
| 2001–2010                     | 15             | 45 155              | 3205         | 8.93 (6.62–11.23)      | 98.7    | <0.001           | 0.09       | 0.05      |                    |
| 2011–2018                     | 26             | 6 566 173           | 778 265      | 10.66 (8.11–13.21)     | 99.9    | <0.001           | 0.17       | 0.03      |                    |

| BMI groupa                    |                |                     |              |                        |         |                  |            |           |                    |
|-------------------------------|----------------|---------------------|--------------|------------------------|---------|------------------|------------|-----------|--------------------|
| Overall                       | 10             | 11 861              | 1165         | 8.43 (7.94–8.93)       | 96.1    | <0.001           | <0.01      | 0.1       | <0.01             |
| Normal weight                 | 2              | 7957                | 684          | 7.64 (3.53–11.74)      | 97.7    | <0.001           | NA         | NA        | NA                 |
| Overweight                    | 4              | 2389                | 258          | 9.75 (4.05–15.45)      | 96.2    | <0.001           | NA         | NA        | NA                 |
| Obesity                       | 4              | 1515                | 223          | 14.27 (5.30–23.24)     | 96.8    | <0.001           | NA         | NA        | NA                 |

| Family history of diabetes    |                |                     |              |                        |         |                  |            |           |                    |
|-------------------------------|----------------|---------------------|--------------|------------------------|---------|------------------|------------|-----------|--------------------|
| Overall                       | 11             | 30 458              | 1556         | 6.66 (5.43–7.89)       | 93.2    | <0.001           | 0.04       | 0.04      | <0.01             |
| Yes                           | 5              | 13 697              | 655          | 7.59 (4.79–10.39)      | 88.9    | <0.001           | NA         | NA        | NA                 |
| No                            | 6              | 16 761              | 901          | 6.80 (4.71–8.89)       | 95.4    | <0.001           | NA         | NA        | NA                 |

| Diagnostic criteriab          |                |                     |              |                        |         |                  |            |           |                    |
|-------------------------------|----------------|---------------------|--------------|------------------------|---------|------------------|------------|-----------|--------------------|
| Overall                       | 48             | 6 630 296           | 781 596      | 8.84 (6.74–10.95)      | 99.9    | <0.001           | 0.02       | <0.01     | <0.01             |
| A                             | 6              | 32 753              | 1201         | 2.12 (0.29–3.95)       | 99.2    | <0.001           | NA         | NA        | NA                 |
| B                             | 21             | 57 215              | 3367         | 8.28 (6.67–9.89)       | 99      | <0.001           | <0.01      | 0.31      |                    |
| C                             | 7              | 10 153              | 1511         | 12.06 (5.70–18.41)     | 99      | <0.001           | NA         | NA        | NA                 |
| D                             | 5              | 6 506 262           | 774 006      | 13.67 (9.08–18.27)     | 99.8    | <0.001           | NA         | NA        | NA                 |
| E                             | 3              | 4327                | 909          | 17.08 (10.16–24.01)    | 95.4    | <0.001           | NA         | NA        | NA                 |

(Continues)
tests were used to estimate differences among subgroups and the trend of pooled prevalence, respectively. When more than 10 studies were included in a single analysis, publication bias was assessed by the Egger linear regression and the Begg rank correlation tests. To detect single studies with disproportionate influence, we conducted a leave-1-out sensitivity analysis for each meta-analysis. Statistical significance was set at $P < 0.05$. Analyses involved use of Stata 11.0 (StataCorp).

## 3 | RESULTS

### 3.1 | Literature search and study characteristics

Of the 9948 potentially relevant studies identified through the database search, 48 articles were included in the final analysis (Figure 1). The details of eligible studies are shown in Table S4 in Appendix S1. A total of 6 630 296 participants were included in the analysis. The total prevalence of prediabetes ranged from 0.25% to 23.47% over the previous decades. A total of 30 of the included studies presented the prevalence data of both sexes; 21 of 48 studies were conducted in the HIC, 11 in the UMIC, and 16 in the LMIC. In all, 16 studies were from the AMR, 9 from the EMR, 9 from the WPR, 6 from the SEAR, 5 from the AFR, and 3 from the EUR. All the included literature had a quality score of at least six.

### 3.2 | Pooled and stratified prevalence of childhood prediabetes

Table 1 shows the overall results. Significant heterogeneity was found among studies ($I^2 = 99.9$, $P < 0.01$;
This finding indicates that older age may be a risk factor for childhood prediabetes. The development of prediabetes was seen more frequently in boys than in girls, suggesting that obesity levels between males and females may explain the higher prediabetes prevalence we found in males. Our study demonstrated an upward trend in prediabetes prevalence in children with increased BMI. This finding is consistent with previous studies showing that obesity may be a risk factor for prediabetes, although one study found no relationship between obesity and prediabetes. The finding of a lower prevalence of prediabetes in rural areas compared with that in urban areas in this study is consistent with published data in China and Vietnam. Aging and growing obesity levels that accompany urbanization may therefore represent precursors to a global prediabetes epidemic. In another study, prevalence of IFG was 88% for those with family history compared to 1.9% for those without, similar to our study and the Cameron County Hispanic Cohort data. For WHO and WB regions, EUR and HIC yielded the lowest pooled prevalence. Differences in dietary habits, lifestyle, and sociodemographic factors among residents of different economic regions may explain these findings. The lowest pooled prevalence with criterion A may be explained by the highest cutoff point of fasting plasma glucose in this criterion compared with the other criteria.

4 | DISCUSSION

In this study, we describe the global prevalence of childhood prediabetes based on published data from 1996 to 2021. Over that period, a rapidly growing trend in childhood prediabetes prevalence was observed. The prevalence increased with BMI and was higher in males than in females, in older compared to younger children, in urban areas compared to rural areas, and in children with family histories of diabetes compared to those without such a history.

Consonant with a national Korean study, we concluded an increase in the prevalence of childhood prediabetes at the global level. The increase in prediabetes prevalence worldwide may be associated with several factors. A positive association between prevalence of childhood prediabetes and age was observed in our study, which is consistent with a national investigation in Saudi Arabia. This finding indicates that older age may be a risk factor for childhood prediabetes. The development of prediabetes was seen more frequently in boys than in girls, suggesting that obesity levels between males and females may explain the higher prediabetes prevalence we found in males. Our study demonstrated an upward trend in prediabetes prevalence in children with increased BMI. This finding is consistent with previous studies showing that obesity may be a risk factor for prediabetes, although one study found no relationship between obesity and prediabetes. The finding of a lower prevalence of prediabetes in rural areas compared with that in urban areas in this study is consistent with published data in China and Vietnam. Aging and growing obesity levels that accompany urbanization may therefore represent precursors to a global prediabetes epidemic. In another study, prevalence of IFG was 88% for those with family history compared to 1.9% for those without, similar to our study and the Cameron County Hispanic Cohort data. For WHO and WB regions, EUR and HIC yielded the lowest pooled prevalence. Differences in dietary habits, lifestyle, and sociodemographic factors among residents of different economic regions may explain these findings. The lowest pooled prevalence with criterion A may be explained by the highest cutoff point of fasting plasma glucose in this criterion compared with the other criteria.

4.1 | Strengths and limitations

The current systematic review and meta-analysis systematically synthesized the global prevalence of childhood prediabetes. Data were analyzed according to a common protocol, while the characteristics and quality of data sources were rigorously verified through repeated checks by two reviewers (Q.S. and C.H.). Moreover, the study provides further strong evidence of the differences associated with gender, age, setting, BMI, family history of diabetes, WHO regions, and WB regions in relation to prediabetes. Many other factors are associated with prediabetes in children, including physical activity,
lifestyle, vitamin D, depression, and education level. We could not, however, perform the combined analysis including these factors because of limited data. Despite an extensive search, the selection bias of our study may have led to an overestimation or underestimation of the prevalence of prediabetes at the global level. HbA1c criteria were associated with higher diagnosis rates of prediabetes than fasting plasma glucose and oral glucose tolerance tests in nondiabetic American children and adults; however, most of the included studies used only fasting plasma glucose to detect prediabetes, possibly underestimating the prevalence of prediabetes. Our review combined the prevalence rates of prediabetes for the included studies with different definitions based on the method applied by some meta-analyses. Subgroup meta-analysis by diagnosis criteria demonstrates the prevalence difference among diagnostic methods. This may have increased uncertainty intervals because of limited comparability. Sensitivity analysis showed that no single study had a disproportionate influence on the pooled prevalence. Our study established an overall combined estimate of prediabetes prevalence as other studies, although heterogeneity of included studies is obstructive. To discover potential sources of heterogeneity, we performed subgroup meta-analysis in limited groups but found that heterogeneity of the subgroups is also substantial. Because of these limitations, we cannot draw more robust and precise conclusions at this time.

The increase in global prevalence of prediabetes over time is an intermediate stage in the progression of type 2 diabetes mellitus and a major risk factor for cardiovascular disease. In a meta-analysis that included four randomized controlled trials with children, a marked mean reduction in fasting insulin and BMI was observed among participants given metformin (with and without lifestyle intervention) compared to those receiving a placebo after at least 2 months. A randomized controlled trial has demonstrated that intensive lifestyle modification can improve insulin resistance in obese children with prediabetes.

Intensive lifestyle modification could help to decrease the prevalence and complication of prediabetes. Further longitudinal studies based on large representative samples should identify risk factors and specific biomarkers of prediabetes in childhood so that early targeted intervention strategies can be developed to delay the inexorable increase in prediabetes and related diseases and decrease the cost burden of health care.

5 | CONCLUSIONS

This study demonstrated that elevated prediabetes prevalence in childhood reaches a considerable level in the world. Intensive lifestyle modification is needed to respond to the prediabetes epidemic globally in the pediatric population.

AUTHOR CONTRIBUTIONS

Jiang and Hu had full access to all the data in the study and take responsibility for the integrity of the data and the accuracy of the data analysis; Han, Jiang, and Hu conceived and designed the meta-analysis; Han and Song drafted the manuscript; Han, Song, Ren, Chen, Jiang, and Hu acquired, analyzed, and interpreted the data or revised the manuscript. All authors read and approved of the final manuscript.

CONFLICT OF INTEREST

No financial conflict or other relationship for each author to be declared.

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**SUPPORTING INFORMATION**

Additional supporting information can be found online in the Supporting Information section at the end of this article.

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