Gestational Diabetes Mellitus Among Asians – A Systematic Review From a Population Health Perspective

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Objective: Since Asians are particularly vulnerable to the risk of gestational diabetes mellitus (GDM), the life course health implications of which are far beyond pregnancy, we aimed to summarize the literature to understand the research gaps on current GDM research among Asians.

Methods: We systematically searched the articles in PubMed, Web of Science, Embase, and Scopus by 30 June 2021 with keywords applied on three topics, namely “GDM prevalence in Asians”, “GDM and maternal health outcomes in Asians”, and “GDM and offspring health outcomes in Asians”.

Results: We observed that Asian women (natives and immigrants) are at the highest risk of developing GDM and subsequent progression to type 2 diabetes among all populations. Children born to GDM-complicated pregnancies had a higher risk of macrosomia and congenital anomalies (i.e. heart, kidney and urinary tract) at birth and greater adiposity later in life.

Conclusion: This review summarized various determinants underlying the conversion between GDM and long-term health outcomes in Asian women, and it might shed light on efforts to prevent GDM and improve the life course health in Asians from a public health perspective.

Systematic Review Registration: Prospero, CRD42021286075.

Keywords: gestational diabetes mellitus, Asians, prevalence, diagnostic criteria, diagnostic guidelines, maternal health outcomes, offspring health outcomes

INTRODUCTION

Diabetes is a significant cause of morbidity, mortality, and healthcare costs worldwide (1). The global age-adjusted comparative prevalence of diabetes among adults between 20-79 years of age was estimated at 8.3% (463 million) in 2019 (2), including 223 million women living with diabetes. And it is projected to reach 700 million people and 343 million women alone in 2045, respectively (2). Diabetes in pregnancy is similarly increasing in prevalence, with concerning consequences for
both mother and offspring (3). Approximately 1 in 6 live births is affected by diabetes in pregnancy, 84% of which are diagnosed as gestational diabetes mellitus (GDM) (2, 4).

GDM is defined as glucose intolerance with the first onset or recognition during pregnancy (2, 4). Women with GDM have higher risks of cardiometabolic disorders during pregnancy and later in life (5). At the same time, offspring born to women with a history of GDM also encounter increased risks of developing obesity and other cardiometabolic disorders later in life (6, 7). The documented prevalence of GDM varies substantially worldwide, ranging from 1% to >30% (3), while compelling evidence has shown Asians share a high prevalence (i.e., Middle East: 8.8-20.0%; South-East Asia: 9.6-18.3%; Western Pacific: 4.5-20.3%) (3) regardless of the racial/ethnic differences in body mass index (BMI).

A meta-analysis found a more than sevenfold increased risk of T2DM in women with GDM after index pregnancy, compared with women with normoglycaemic pregnancies (8). Data on risk factors—particularly modifiable risk factors that may inform effective intervention strategies—are relatively more collected in the Western population (e.g., North America, Europe, and Oceania) than the Asian population (3, 8-10). Research reporting a full spectrum of long-term health outcomes among both mothers and offspring following pregnancies complicated by GDM also mainly stemmed from the Western population (11). Furthermore, GDM studies have not been comprehensively reviewed on Asian immigrants exclusively, given that an increasing number of Asian migrants live in Western countries for a long-term residency (12). Due to the different environmental exposures such as socioeconomic transitions, lifestyle adaptations, cultural assimilation hardship, and health disparities, there might be exceptionally high attributable risks on GDM development for Asian immigrants compared with Native Asians.

This review sought to summarize the literature to understand research gaps and develop future research directions on Asian women with GDM from a population health perspective. Thus, our review serves the objectives to 1) comprehensively examine the epidemiology of GDM, its risk factors, and health consequences; and 2) identify areas for future research for public health interventions to prevent GDM and its health consequences.

**METHODS**

**Search Strategy and Selection Criteria**

We conducted the systematic review according to PRISMA for systematic review protocols. References for this review were identified through searches of Pubmed, Web of Science, Embase, and Scopus for articles published until 30 June 2021. We included three topics in our review, namely “Topic 1—GDM prevalence in Asians”, “Topic 2—GDM and maternal health outcomes in Asians”, and “Topic 3—GDM and offspring health outcomes in Asians”. Search terms included “prevalence”, “incidence”, “gestational diabetes mellitus”, “gestational diabetes” and “diabetes in pregnancy” in combination with the terms “Asia”, “Asians” and “Asian countries” in Topic 1. Search terms included “gestational diabetes mellitus”, “gestational diabetes” and “diabetes in pregnancy” in combination with the terms “Type 2 diabetes”, “prediabetes”, “glucose intolerance”, “abnormal glucose”, “hypertension”, “high blood pressure”, “cardiovascular disease”, “kidney disease”, “cancer”, “liver dysfunction”, “non-alcoholic fatty liver disease” and “health outcomes” and also in combination with the terms “After delivery” and “postpartum” in Topic 2. Search terms included “gestational diabetes mellitus”, “gestational diabetes”, “diabetes in pregnancy” and in combination with terms “cardio-metabolic outcome”, “cognitive outcome”, “congenital disease”, “adiposity”, “hypertension”, “health outcome”, “neuro-cognitive outcome”, “obesity”, “diabetes”, “cardiovascular disease”, “kidney disease” and “cancer” and also in combination with “child” and “offspring” in Topic 3. Articles resulting from these searches and relevant references cited in those articles were reviewed, among which reporting non-Asian human subjects or without full-text available were excluded. Flow charts for literature searching on each topic are shown in Supplementary Figures 1-3. The Prospero registration number for this systematic review is registered as CRD42021286075.

**Data Screening & Assessments**

Double literature screening was conducted during the literature searching phase by two investigators (H L & L-J L). Furthermore, one investigator (A C) performed the quality assessments for all papers based on the Newcastle–Ottawa Scale Criteria (NOSC), and the other investigators (L-J L) verified the findings independently. The maximum score of 9 points in the Newcastle–Ottawa Scale is distributed in three aspects, namely selection of study groups (four points), comparability of groups (two points), and ascertainment of exposure and outcomes (three points) for case–control and cohort studies (13). We used the points to further categorize the publication quality with low risk of bias (between 7-9 points), high risk of bias (between 4-6 points), and very high risk of bias (between 0-3 points) (Supplementary Tables 1, 2).

**RESULTS**

**Prevalence of GDM by Geography**

**Overview**

GDM prevalence in Asian countries ranges widely from 1.2 to 49.5%, largely accounting for differences in diagnostic criteria, sample size and population source (e.g., hospital-based, community-based) (Figure 1 and Supplementary Table 3).

**Guideline-Specific Prevalence of GDM**

The prevalence of GDM varied substantially across Asian countries using different guidelines (Figure 2). We identified 29 GDM diagnostic criteria (Supplementary Table 4), among which the International Association of Diabetes and Pregnancy Study Groups (IADPSG) (14), World Health Organization (WHO) (15), Carpenter-Coustan (16), and American College of Obstetricians and Gynecologists (ACOG) (17) criteria were
commonly used. Some countries adopted international guidelines as their national guidelines [e.g., China MOH guidelines (18), Malaysia MOH guidelines (19)], while some countries defined their own [e.g., Japan Japan Diabetes Society (20), India [Diabetes in Pregnancy Study group of India; DIPS1] (21), Turkmenistan (22), Oman (23)]. As the majority (123 out of 147) of included studies were published since 2010, we were not able to tease out whether the increment in GDM prevalence over the years in Asians is due to emerging evidence or new adoption of universal screening [i.e., IADPSG (14)].

We included studies using either one-step or two-step diagnostic guidelines, the latter of which performed a 1-h 50-g glucose challenge test (GCT) glucose challenging test (GCT) additionally during 24-28 weeks of gestation, with a whole blood glucose threshold of 7.2 mmol/l (130 mg/dl). In general, we observed a link between adopting any one-step diagnostic guidelines (e.g., the IADPSG guidelines, the WHO 1999 guidelines) and higher GDM prevalence among Asian studies.

For example, countries exclusively using (e.g., Singapore, UAE) or primarily using (e.g., China, Saudi Arabia, India) a one-step diagnostic approach reported an overall GDM prevalence above 10%. In contrast, countries exclusively using (e.g., Pakistan, South Korea) or primarily using (e.g., Thailand, Turkey, Japan) a two-step diagnostic approach reported an overall GDM prevalence below 10% (Figure 3).

**Prevalence of GDM in Asian Migrants**
Twenty-eight studies reported GDM prevalence among Asian migrants in Europe, Oceania, and North America, with sample sizes ranging from 1,491 to 10,823,924 participants. Overall GDM prevalence among Asian migrants is comparable to the Native Asian population. However, the prevalence of GDM was generally higher in Asian immigrants (0.18%-24.2%) than non-Hispanic White (NHW) (0.02%-7.0%) living in the same country, regardless of GDM diagnostic guidelines used (Supplementary Table 5). Among Asian immigrants in UK
and Norway, South, East, and West Asian immigrants, as a whole, had doubled the odds for GDM than NHW (24, 25). Interestingly, length of immigration and birth countries seemed to relate to GDM prevalence. For instance, Danish-Chinese migrants with a longer stay (≥ 10 years) had a 62% higher odds of GDM onset than those with a shorter stay (≤ 5 years) (26). Also, foreign-born US-Indian migrants had a higher GDM prevalence than local-born US-Indian migrants (22.9% vs. 12.8%) (27).

**Adverse Health Outcomes and Attributable Risk Factors Following an Index GDM-Complicated pregnancy**

**Overview**

Overall, seventy-two studies, predominantly longitudinal cohorts on GDM and maternal postpartum health outcomes, were identified in Asian countries (Table 1 and Figure 4). Among them, prediabetes and T2D, cardiovascular disorders, cancer, and non-alcoholic fatty liver disease (NAFLD) were reported following index pregnancy complicated by GDM, with a mean or median follow-up from 4 weeks to 38 years after delivery. The majority of studies were reported from East Asia (42/72 studies, 58.3%), especially in the Chinese population. Two studies that reported postpartum T2D development in Asian immigrants were identified (Supplementary Table 6). Thirteen out of 74 included studies (18%) were assessed low in risk of bias, while the rest majority (80%) were either high or very high risk of bias (Supplementary Table 1).

**Prediabetes and T2D**

It is well-known that women with a history of GDM have a substantially increased risk of developing T2D than counterparts without such a history (8). A systematic review and meta-analysis on prospective studies with reasonable retention rates (mainly on European women) suggested that the conversion rate from GDM to T2D was seven folds increased among women GDM after index pregnancy, compared with those who had a normoglycaemic pregnancy (RR 7.43, 95% CI: 4.79-11.51) (8).

Sixty-three studies described the postpartum incidence rate of prediabetes and T2D among mothers diagnosed with GDM in Asia, with sample sizes ranging from 35 to 11 270 subjects, most of which defined prediabetes and T2D using the same guidelines [e.g., WHO 1999 (41) or ADA 2014 guidelines (42)] even though their GDM diagnostic criteria differed. We reported the percentage incidence (%) if prediabetes or T2D was recorded within one year from delivery (mostly between 6 and 12 weeks). Then we reported person-years incidence (per 1000 person-years) if prediabetes or T2D was recorded beyond one year from delivery (up to 15 years).

Within one year from delivery, the conversion rate varied significantly between studies from GDM to prediabetes (11.9%-49.1%) and from GDM to T2D (1.1%-66.7%), respectively. Beyond one year after delivery, the incidence rate from GDM to T2D was the highest in South Asia (47–271 per 1000 person-years), followed by East Asia (9–110 per 1000 person-years). We noted inconsistencies with study estimates within the same region. For instance, one study in Iran reported a much higher incidence T2D conversion rate than another study in Iran (172 vs. 9 per 1000 person-years) (35, 43). Potential reasons for inconsistencies in the conversion rates from GDM to T2D could be the variation in studied population characteristics, duration of follow-up, retention rate, and data collection quality.

As for Asian immigrants, we identified only two reports comparing Asian immigrants with non-Asian counterparts, one from Spain with one-year follow-up (44) and the other from the US with an average 7.6-year follow-up (45). Both studies suggested that prediabetes and T2D conversion rates were higher in South Asian migrants than native NHW [prediabetes: 43.3% vs. 28.5% (44); T2D: 55 vs. 40 per 1000 person-years (45)].

Existing data on risk factors of T2D among women with a history of GDM were firstly reported in the NHW population,
| Maternal Health Outcome | Country | No. | PMID | Author Year | Study design | Mean or range of follow-up | No. of GDM | No. of outcome cases | Cumulative incidence rate; Incidence rate (per 1000 person-years) if applicable* | Baseline age, years | Baseline BMI, kg/m² | GDM diagnosis guidelines | Outcome diagnostic guidelines |
|------------------------|---------|-----|------|-------------|--------------|-----------------------------|-----------|----------------------|--------------------------------|-----------------|------------------|----------------------|--------------------------|
| Pre-diabetes and T2D  | China   | 1   | 3309614 | Pei et al., 2021 | Retrospective cohort study | 6-12 weeks | 589 | Pre-diabetes: 191 | T2D: 3.1% | Pre-diabetes: 32.4% | T2D: 3.1% | 33-34 (follow-up) | IADPSG WHO 1999 |
|                        |         |     |       |             |              |                             |           |                      |                                |                |                  |                      |                          |
|                        | China   | 2   | 3251565 | Mao et al., 2020 | Cross-sectional | 1.5 year | 425 | Pre-diabetes: 62 | T2D: 27 | Pre-diabetes: 14.6%; T2D: 6.3%; 42 | 32.3 | >24: 69.2%; 24-27.9: 24.7%; >28: 6.1% | Did not define | WHO 1999 |
|                        | China   | 3   | 3208017 | Mao et al., 2020 | Prospective cohort | 5.5 years | 55 | Pre-diabetes: 19 | T2D: 9 | Pre-diabetes: 34.6%; T2D: 16.4%; 30 | 31 | <25: 78.0%; >25: 22.0% | NDDG & IADPSG Chinese | WHO 1998 |
|                        | China   | 4   | 3119619 | Wang et al., 2019 | Prospective cohort | 6-12 weeks | 563 | Pre-diabetes: 157 | T2D: 17 | Pre-diabetes: 26.9%; N.A. | 32.5 | <18.5: 16.0%; <18.5-24: 69.6%; >25: 14.3% | MOH IADPSG | WHO 1999 |
|                        | China   | 5   | 3099688 | Liu et al., 2019 | Prospective cohort | 6 months | 91 | Pre-diabetes: 27 | T2D:  | Pre-diabetes: 29.7%; N.A. | T2D: 1.1%; N.A. | 32.7 | <18.5: 16.0%; <18.5-24: 69.6%; >25: 14.3% | IADPSG | WHO 1999 |
|                        | China   | 6   | 3147216 | Fan et al., 2019 | Prospective cohort | 4.22 years | 1063 | Pre-diabetes: 457 | T2D: 114 | Pre-diabetes: 36.2%; T2D: 9.0%; 86 | 32.4 | 23.1 | WHO 1999 | WHO 1999 |
|                        | China   | 7   | 3018271 | Ma et al., 2018 | Prospective cohort | 6-8 weeks | 399 | T2D: 9 | T2D: 2 | Pre-diabetes: 75.3%; T2D: 25.6%; N.A. | 31.3 | 23.1 | IADPSG | WHO 1999 |
|                        | China   | 8   | 2439739 | Mai et al., 2014 | Case-control study | 2.5 years | 190 | Pre-diabetes: 121 | T2D: 57 | Pre-diabetes: 26.7%; T2D: 12.1%; N.A. | 33.1 | 22.7 | ADA 2004 | ADA 2010 |
|                        | China   | 9   | 2527112 | Chang et al., 2014 | Prospective cohort | 6-12 weeks | 282 | Pre-diabetes: 157 | T2D: 17 | Pre-diabetes: 26.9%; N.A. | T2D: 2.9%; N.A. | 29.6 | 26.2 | ADA 2004 | ADA 2007 |
|                        | Taiwan  | 10  | 1870121 | Cao et al., 2016 | Prospective cohort | 6-6 weeks | 186 | Pre-diabetes & T2D: 52 | T2D: 29 | Pre-diabetes & T2D: 28.0%; N.A. | T2D: 40.8%; N.A. | 31.7 | 24.9 | NDGG ICD | |
|                        | Taiwan  | 11  | 2586528 | Lin et al., 2016 | Retrospective cohort study | 6 months - 9 years | 71 | Pre-diabetes: 182 | T2D: 105 | Pre-diabetes: 22.7%; N.A. | T2D: 13.1%; N.A. | 34 | 24.8 | Abell and Beischer criteria | WHO 1985 |
|                        | Taiwan  | 12  | 1870121 | Cao et al., 2016 | Prospective cohort | 6-8 weeks | 186 | Pre-diabetes & T2D: 52 | T2D: 29 | Pre-diabetes & T2D: 28.0%; N.A. | T2D: 40.8%; N.A. | 31.7 | 24.9 | NDGG ICD | |
|                        | Taiwan  | 13  | 2213984 | Tam et al., 2012 | Retrospective cohort study | 36 months | 170 | T2D: 9 | T2D: 21 | Pre-diabetes: 5.3%; 18 | T2D: 9.0%; 21 | 24.4 | 24.7 | WHO 1999 | WHO 1999 |
|                        | Taiwan  | 14  | 2166867 | Lee et al., 2012 | Retrospective cohort study | 52 months | 238 | T2D: 9 | T2D: 21 | Pre-diabetes: 5.3%; 18 | T2D: 9.0%; 21 | 24.4 | 24.7 | WHO 1999 | WHO 1999 |
|                        | Taiwan  | 15  | 1468769 | Ko et al., 1999 | Prospective study | 6 weeks | 801 | Pre-diabetes: 182 | T2D: 105 | Pre-diabetes: 22.7%; N.A. | T2D: 13.1%; N.A. | 34 | 24.8 | Abell and Beischer criteria | WHO 1985 |
|                        | Japan    | 16  | 3199629 | Kasawaki et al., 2020 | Retrospective cohort study | 1 year | 399 | Pre-diabetes: 182 | T2D: 105 | Pre-diabetes: 22.7%; N.A. | T2D: 13.1%; N.A. | 34.1 | 23.4 | JSOG/IADPSG | JSOG | AIDPSG | |
|                        | Japan    | 17  | 3025396 | Kasuga et al., 2019 | Prospective cohort study | 24.9 weeks | 213 | Pre-diabetes: 51 | T2D: 8 | Pre-diabetes: 23.9%; T2D: 3.8%; N.A. | 34.1 | 23.4 | JSOG/IADPSG | JSOG | |
|                        | Japan    | 18  | 2969644 | Inoue et al., 2018 | Prospective cohort study | 2 years | 77 | Pre-diabetes: 17 | T2D: 17 | Pre-diabetes: 22.1%; 110 | T2D: 22.1%; T2D: 110 | 34.3 | 23.9 | IADPSG | WHO 1998 |
|                        | Japan    | 19  | 2970619 | Kondo et al., 2018 | Prospective cohort study | 8-12 weeks | 123 | Pre-diabetes: 41 | T2D: 4 | Pre-diabetes: 33.3%; T2D: 3.3%; N.A. | 34 | 21.4 | IADPSG | WHO 1999 |
|                        | Japan    | 20  | 2301007 | Kugishima et al., 2018 | Retrospective cohort study | 1.09 years | 306 | Pre-diabetes: 182 | T2D: 105 | Pre-diabetes: 22.7%; N.A. | T2D: 13.1%; N.A. | 34 | 21.4 | IADPSG | WHO 1999 |
|                        | Japan    | 21  | 2062402 | Nishikawa et al., 2018 | Prospective cohort study | 6-12 weeks | 185 | Pre-diabetes: 22 | T2D: 3 | Pre-diabetes: 11.9%; T2D: 1.6%; N.A. | 33.05 | 23.5 | JSGO/IADPSG | JSGO | |
|                        | Japan    | 22  | 2872525 | Yasuhi et al., 2017 | Prospective cohort study | 1 year | 88 | Pre-diabetes: 29 | T2D: 13 | Pre-diabetes: 33.0%; N.A. | T2D: 14.8%; N.A. | 33.3 | 23.9 | JSGO/IADPSG | JSGO | |
|                        | Japan    | 23  | 2549788 | Kugishima et al., 2015 | Prospective cohort study | 6-8 weeks | 169 | Pre-diabetes: 27 | T2D: 17 | Pre-diabetes: 29.7%; N.A. | T2D: 11.9%; N.A. | 32.6 | 23.5 | JSGO/IADPSG | JSGO | |

(Continued)
| Maternal Health Outcome | Country | No | PMID | Author | Year | Study design | Mean or range of follow-up | No of GDM | No of outcome cases | Cumulative incidence rate; Incidence rate (per 1000 person-years) if applicable* | Baseline age, years | Baseline BMI, kg/m² | GDM diagnosis guidelines | Outcome diagnostic guidelines |
|-------------------------|---------|----|------|--------|------|--------------|---------------------------|----------|-------------------|----------------------------------|-----------------|----------------|----------------|-----------------------------|
| South Korea | 24 | 30486265 | Han et al., 2018 | 2018 | Retrospective cohort study | 10 years | 4970 | Pre-diabetes: 52 | T2D: 470 | Pre-diabetes: 30.8% | T2D: 3.6%; T2D: 9.5%; 9 | 28.3 | 21 | JSOG/IADPSG | ICD-10 ICD-10 |
| | 25 | 27583868 | Cho et al., 2016 | 2016 | Prospective cohort | 3.98 years | 412 | T2D: 51 | 2962 | T2D: 12.4%; 31 | T2D: 8.4%; 11 | 30.6 | 23.5 | NDGG ADA 2010 | |
| | 26 | 27159192 | Cho et al., 2016 | 2016 | Prospective cohort | 8 years | 699 | Pre-diabetes: 343 | T2D: 36 | Pre-diabetes: 49.1%; N.A. | T2D: 5.2%; N.A. | 29.9 | 21.7 | ICD-10 ICD-10 | |
| | 27 | 26996814 | Kim et al., 2016 | 2016 | Prospective cohort | 6-12 weeks | 498 | Pre-diabetes: 157 | T2D: 40 | Pre-diabetes: 31.5%; N.A. | T2D: 8.0%; N.A. | 33.3 | 23.7 | CC | ADA 2004 |
| | 28 | 26674320 | Shin et al., 2016 | 2016 | Prospective cohort | 8 years | 2962 | T2D: 249 | 249 | T2D: 8.4%; 11 | T2D: 8.0%; N.A. | 29.9 | 21.7 | ICD-10 ICD-10 | |
| | 29 | 26713061 | Cho et al., 2015 | 2015 | Retrospective cohort study | 6-12 weeks | 757 | Pre-diabetes: 334 | T2D: 139 | Pre-diabetes: 44.1%; N.A. | T2D: 18.4%; N.A. | 33.7 | 23.7 | CC | ADA 2011 |
| | 30 | 26171796 | Moon et al., 2015 | 2015 | Prospective cohort | 4 years | 283 | Pre-diabetes: 129 | T2D: 33 | Pre-diabetes: 44.1%; N.A. | T2D: 18.4%; N.A. | 33.7 | 23.7 | NDGG ADA 2010 | |
| | 31 | 24431910 | Yang et al., 2014 | 2014 | Prospective cohort | 15.6 months (1.3 years) | 116 | Pre-diabetes: 59 | T2D: 8 | Pre-diabetes: 50.9%; 39 | T2D: 6.9%; 53 | 33.8 | 23.7 (follow-up) | NDGG ADA 2010 | |
| | 32 | 23471980 | Kwak et al., 2013 | 2013 | Prospective cohort | 1 year | 370 | Pre-diabetes: 88 | T2D: 88 | Pre-diabetes: 50.9%; 39 | T2D: 6.9%; 53 | 33.8 | 23.7 (follow-up) | NDGG ADA 2010 | |
| | 33 | 24057154 | Kwak et al., 2013 | 2013 | Prospective cohort | 3.75 years | 395 | T2D: 116 | T2D: 88 | T2D: 20.8%; N.A. | T2D: 8.0%; N.A. | 32 | 23 | CC | ADA 2014 |
| | 34 | 21106349 | Kim et al., 2011 | 2011 | Prospective cohort | 6-12 weeks | 381 | Pre-diabetes: 161 | T2D: 27 | Pre-diabetes: 42.3%; N.A. | T2D: 7.1%; N.A. | 34.2 | 23.6 | CC | ADA 2004 |
| | 35 | 18456364 | Lee et al., 2008 | 2008 | Prospective cohort | 2.1 years | 620 | Pre-diabetes: 21 | T2D: 71 | Pre-diabetes: 11.5%; 55 | T2D: 17.0%; 42 | 33.6 | 23.5 | NDGG ADA 2011 | |
| | 36 | 17256060 | Lim et al., 2007 | 2007 | Prospective cohort | 1 year | 81 | Pre-diabetes: 21 | T2D: 71 | Pre-diabetes: 11.5%; 55 | T2D: 17.0%; 42 | 33.6 | 23.5 | NDGG ADA 2011 | |
| | 37 | 16054264 | Cho et al., 2006 | 2006 | Prospective cohort | 6 years | 909 | Pre-diabetes: 59 | T2D: 120 | Pre-diabetes: 50.9%; 39 | T2D: 6.9%; 53 | 33.8 | 23.7 (follow-up) | NDGG ADA 2011 | |
| | 38 | 12951280 | Jang et al., 2003 | 2003 | Prospective cohort | 6-8 weeks | 311 | Pre-diabetes: 72 | T2D: 47 | Pre-diabetes: 23.2%; 22 | T2D: 10.1%; N.A. | 30.9 | 22.7 | Korean guidelines | |
| Thailand | | 39 | 29926712 | Ruksasakul et al., 2012 | 2012 | Case-control | 2.97 years | 56 | Pre-diabetes: 29 | T2D: 47 | Pre-diabetes: 23.2%; 22 | T2D: 10.1%; N.A. | 30.9 | 22.7 | Korean guidelines | |
| | 40 | 23692133 | Youngwanitchsera et al., 2013 | 2013 | Cross-sectional | 6 weeks | 210 | Pre-diabetes: 56 | T2D: 47 | Pre-diabetes: 23.2%; 22 | T2D: 10.1%; N.A. | 30.9 | 22.7 | Korean guidelines | |
| Malaysia | 41 | 23208155 | Chew et al., 2012 | 2012 | Cross-sectional study | 84 months (7 years) | 342 | T2D: 53 | T2D: 15.5%; 22 | T2D: 15.5%; 22 | 34.7 | 23.7 (follow-up) | ADA 2010 WHO 1985 | |
| | 42 | 33525398 | Hewage et al., 2021 | 2021 | Prospective cohort | 1 year | 116 | Pre-diabetes: 38 | T2D: 13 | Pre-diabetes: 32.8%; 38 | T2D: 11.2%; 11 | 33.3 | 23.7 | WHO 1999 WHO 1999 | |
| Philippines | 43 | N/A | Malong et al., 2013 | 2013 | Prospective cohort | 3 years | 124 | Pre-diabetes: 43 | T2D: 9 | Pre-diabetes: 34.7%; 116 | T2D: 7.3%; 24 | 32.1 | 23.8 | IADPSG/CC/WHO | ADA 2004 |

(Continued)
| Maternal Health Outcome | Country | No | PMID | Author | Year | Study design | Mean or range of follow-up | No of GDM | No of outcome cases | Cumulative incidence rate; Incidence rate (per 1000 person-years) if applicable* | Baseline age, years | Baseline BMI, kg/m² | GDM diagnosis guidelines | Outcome diagnostic guidelines |
|------------------------|--------|----|------|--------|------|--------------|----------------------------|-----------|-------------------|----------------------------------|-----------------|-----------------|---------------------------|--------------------------|
| India                  | 44     | 29802954 | Goyal et al., 2018 | 2018 | Prospective cohort | 20 months (1.7 years) | 267 | Pre-diabetes: 126; T2D: 28 | Pre-diabetes: 47.2%; T2D: 10.5% | 32.5 | 27.3 | IADPSG | ADA 2014, WHO 2006 |
|                       | 45     | 27329018 | Bhavadharini et al., 2016 | 2016 | Prospective cohort | 6 weeks -1 year | 203 | Pre-diabetes: 34; T2D: 7 | Pre-diabetes: 16.7%; T2D: 3.4% | 29.1 | 26.9 | IADPSG | ADA 2005 |
|                       | 46     | 26926329 | Gupta et al., 2017 | 2017 | Prospective cohort | 14 months (1.2 years) | 366 | Pre-diabetes: 114 T2D: 119 | Pre-diabetes: 39.3%; T2D: 21 | 30.2 | <25.0: 67.9; 25.0-29.0: 25.6% > 30.0: 6.3% | IADPSG | ADA 2014, WHO 2006 |
|                       | 47     | 25952037 | Jindal et al., 2015 | 2015 | Prospective cohort | 6 weeks | 62 | Pre-diabetes: 17; T2D: 4 | Pre-diabetes: 27.4%; T2D: 6.5% | 31.5 | not specified | ADA 2011 | ADA 2011 |
|                       | 48     | 24944938 | Mahalakshmi et al., 2014 | 2014 | Prospective cohort | 4.5 years | 174 | Pre-diabetes: 3; T2D: 1 | Pre-diabetes: 25.1%; T2D: 4.1% | 29 | 28.6 | ADA 2005 | WHO 2006 |
|                       | 49     | 17640759 | Krishnaveni et al., 2007 | 2007 | Prospective cohort | 5 years | 35 | Pre-diabetes: 11; T2D: 13 | Pre-diabetes: 31.4%; T2D: 37.1% | 28.2 | 25.5 (follow-up) | WHO 2005 | WHO 2006 |
| Sri Lanka              | 50     | 29679628 | Sudasinghe et al., 2018 | 2018 | Prospective cohort | 1 year | 59 | Pre-diabetes: 17 T2D: 11 | Pre-diabetes: 28.8%; T2D: 18.6% | 30.2 | <25: 8.9%; 25.0-34: 58.0%; 35-49: 33.1%; ≥ 50: not specified | IADPSG | ADA 2014, WHO 2006 |
|                       | 51     | 28644881 | Herath et al., 2017 | 2017 | Prospective cohort | 10.9 years | 119 | T2D: 73 | T2D: 61.3%; T2D: 56 | 31.7 | 27.0 | WHO 2009 | WHO 1999 |
|                       | 52     | 16972962 | Wijeysinghe et al., 2006 | 2006 | Prospective cohort study | 34.6 months (2.9 years) | 147 | Pre-diabetes: 56; T2D: 20 | Pre-diabetes: 38.1%; T2D: 13.6% | 33.4 | 26.3 | WHO 2009 | IDF |
| Pakistan               | 53     | 28423981 | Azz et al | 2018 | Prospective cohort | 2 years | 78 | Pre-diabetes: 3; T2D: 11 | Pre-diabetes: 3.8%; T2D: 14.1% | 28.9 | not specified | IADPSG | Did not define |
| Israel                 | 54     | 31167664 | Yefet et al, 2019 | 2019 | Prospective cohort study | 15.8±5.1 years | 446 | T2D: 207 | T2D: 40.6% | 30.1 | 27.0 | CC and NDDG | ICDD |
|                       | 55     | 20636958 | Chodick et al., 2010 | 2010 | Retrospective cohort study | 5.7 years | 11270 | T2D: 1125 | T2D: 10.0% | 32.7 | <25: 14.6%; 25-30: 16.3%; >30: 20.0% unknown | WHO 2009 | MHS guidelines |
| Turkey                 | 56     | 24591906 | Kerimoglu et al, 2010 | 2010 | Prospective cohort | 6-12 weeks | 78 | Pre-diabetes: 28; T2D: 9 | Pre-diabetes: 35.9%; T2D: 34.6% | 31.3 | 27.7 | CC | WHO 2006 |
| Iran                   | 57     | 28432896 | Minoose et al, 2017 | 2017 | Prospective cohort | 12.1 years | 476 | Pre-diabetes: 27 | Pre-diabetes: 35.8%; T2D: 10.3% | 36.5 | 28.4 | WHO 2009 | ADA 1997 |
|                       | 58     | 28491872 | Nouh et al., 2015 | 2015 | Prospective cohort | 6-12 weeks | 176 | Pre-diabetes: 3 | Pre-diabetes: 35.9% | 29.7 | 27.8 | IADPSG | ADA 2003 |
|                       | 59     | 25692996 | Valizadeh et al., 2014 | 2014 | Prospective cohort | 22.8 months (1.9 years) | 110 | Pre-diabetes: 11; T2D: 12 | Pre-diabetes: 17.6%; T2D: 4.5% | 28.5 | not specified | ADA 2015 | WHO 2006 |
|                       | 60     | 17962102 | Hossein-Nooshad et al., 2009 | 2009 | Retrospective cohort study | 6-12 weeks | 114 | Pre-diabetes: 24; T2D: 9 | Pre-diabetes: 21.4% | 27.4 | CC | ADA/WHO 2008 |
| UAE                    | 61     | 15003951 | Agarwal et al, 2004 | 2004 | Retrospective cohort study | 4-8 weeks | 549 | Pre-diabetes: 20; T2D: 9 | Pre-diabetes: 20.8% | 32 | not specified | ADA 1997 | WHO 1999 |

(Continued)
| Maternal Health Outcome | Country     | No PMID       | Author, Year                                      | Study design          | Mean or range of follow-up | No of GDM | No of outcome cases | Cumulative incidence rate; Incidence rate (per 1000 person-years) if applicable* | Baseline age, years | Baseline BMI, kg/m² | GDM diagnosis guidelines | Outcome diagnostic guidelines |
|-------------------------|-------------|---------------|--------------------------------------------------|-----------------------|---------------------------|-----------|---------------------|---------------------------------------------------------------------------------|-------------------|-------------------|--------------------------|---------------------------|
| Cancer                  | South Korea | 30486285      | Han et al., 2018                                 | Retrospective cohort  | 10 years                  | 4970      | Total cancer: 437   | Thyroid Cancer: 131                                                           | 28.3              | 21                | ICD-10                   | ICD-10                    |
|                         | Taiwan      | 30796123      | Peng et al., 2019                                 | Retrospective cohort  | 6.84 years                | 4737      | Total cancer: 1063  | Breast cancer: 284                                                             | 29.0              | not specified      | ICD-10                   | ICD-10                    |
|                         | Taiwan      | 24820466      | Li et al., 2020                                   | Case-control          | 6-12 weeks                | 589       | Dyslipidaemia:227   | Dyslipidaemia: 38.5%                                                          | 33.1              | 21                | AHA/NHLBI criteria       | NCEP ATP III criteria     |
| Hypertension            | China       | 32157330      | Li et al., 2021                                   | Prospective cohort    | 3.53 years                | 1263      | Mets NCEP ATP III criteria: 246 | Mets by NCEP ATP III criteria: 19.5%; 55                                  | 33-34 (follow-up) | 21.49-21.99 | IADPSG                  | NCEP ATP III criteria     |
|                         | China       | 28060987      | Wang et al., 2017                                 | Prospective cohort    | 2.29 years                | 1261      | Hypertension: 16    | Hypertension: 7.45%; 33                                                        | 32.8              | 24.3              | WHO 1999                 | 2007 ESH, ESCG            |
|                         | China       | 24397392      | Mai et al., 2014                                  | Case-control          | 2.5 years                 | 190       | Hypertension: 16    | Hypertension: 7.45%; 33                                                        | 33.1              | 22.7              | ADA 2004                 | ADA 2010                  |
|                         | China       | 33036614      | Pei et al., 2017                                  | Retrospective cohort  | 6-12 weeks                | 589       | Dyslipidaemia:227   | Dyslipidaemia: 38.5%                                                          | 33.1              | 22.7              | ADA 2004                 | ADA 2010                  |
|                         | China       | 30005506      | Shen et al., 2019                                 | Prospective cohort    | 3.53 years                | 1263      | Mets NCEP ATP III criteria: 246 | Mets by NCEP ATP III criteria: 19.5%; 55                                  | 33-34 (follow-up) | 21.49-21.99 | IADPSG                  | NCEP ATP III criteria     |
|                         | South Korea | 27583868      | Cho et al., 2016                                  | Prospective cohort    | 3.98 years                | 412       | Mets: 38            | Mets: 16.0%; 40                                                               | 33.6              | 23.5              | NDGG                     | ADA 2010                  |
|                         | Thailand    | 29926712      | Ruksasakul et al., 2016                           | Case-control          | 2.97 years                | 56        | Mets: 15            | Mets: 20%; 80                                                                 | 33.1              | 22.7              | ADA 2004                 | ADA 2010                  |
|                         | South Korea | 24397392      | Mai et al., 2016                                  | Case-control          | 2.5 years                 | 190       | Mets: 38            | Mets: 16.0%; 40                                                               | 33.6              | 24.6              | CC                       | AHA/NHLBI criteria         |

70
8

38.6

(Continued)
| Maternal Health Outcome | Country | No | PMID | Author | Year | Study design | Mean or range of follow-up | No of GDM | No of outcome cases | Cumulative incidence rate; Incidence rate (per 1000 person-years) if applicable* | Baseline age, years | Baseline BMI, kg/m² | GDM diagnosis guidelines | Outcome diagnostic guidelines |
|-------------------------|---------|----|------|--------|------|--------------|---------------------------|--------|------------------|--------------------------------|----------------|-----------------|------------------------|-----------------------------|
| Non-Alcoholic Fatty Liver Disease (NAFLD) | India | 72 | 32961610 | Kubhal et al., | 2021 | Cross-sectional | 16 months (9-38 months) | 201 | 26.7% | NAFLD: 62.7%; 63 | 31.9 | 26.3 | IADPSG | Fibroscan |
| Cardiovascular (CV) events | Israel | 71 | 23749791 | Kessous et al., | 2013 | Prospective cohort | 10 years | 4928 | Simple CV events (not specified): 365 | Simple CV events: 7.4%; 741 | 32.4 | NDGG | ICD |
| Cardiovascular (CV) events | Israel | 71 | 23749791 | Kessous et al., | 2013 | Prospective cohort | 10 years | 4928 | Simple CV events (not specified): 365 | Simple CV events: 7.4%; 741 | 32.4 | NDGG | ICD |
| Iran | 58 | 25892996 | Valizadeh et al., | 2015 | Prospective cohort | 22.8 months (1.9 years) | 110 | MetS: 22 | 20%; 105 | >34.64.5% | 28.5 | Did not define | Israelite National Committee Guidelines | Untitled |

N.A., Not available; T2D, type 2 diabetes; HTN, hypertension; MetS, metabolic syndrome; GDM, gestational diabetes mellitus; BMI, body mass index; AHA, American Heart Association; NHLBI, National Heart Lung and Blood Institutes; ICD, International Classification of Diseases; IDF, International Diabetes Federation; NCEP ATPIII, National Cholesterol Education Program Adult Treatment Panel III; ESH-ESC, European Society of Hypertension-European Society of Cardiology Guidelines; MHS, Maccabi Healthcare Services; JSOG, Japan Society of Obstetrics and Gynecology; CC, Carpenter-Coustan; ADA, American Diabetes Association; WHO, World Health Organization; NDDG, National Diabetes Data Group; IADPSG, International Association of Diabetes and Pregnancy Study Groups; MOH, Ministry of Health.

Criteria of Abell and Beischer: GDM was defined as if 3hr 50g OGTT of any 2 abnormal glucose readings: 0-hr ≥5.0 mmol/L; 1-hr ≥9.5 mmol/L; 2-hr ≥8.1 mmol/L; 3-hr ≥7.0 mmol/L.

Korean guidelines: GDM was defined as if 3hr 100g OGTT of any 2 abnormal glucose readings: 0-hr ≥5.8 mmol/L; 1-hr ≥10.6 mmol/L; 2-hr ≥9.2 mmol/L; 3-hr ≥8.1 mmol/L.

Israelite National Committee Guidelines: MetS was defined as having any three of the following traits: waist circumference > 98 cm in females; triglyceride > 150 mg/dL (> 1.70 mmol/L) or drug consumption for elevated triglyceride levels; high-density lipoprotein < 1.30 mmol/L; systolic blood pressure ≥ 130 and/or diastolic blood pressure ≥ 85 mm Hg or receiving antihypertensive drugs; and fasting plasma glucose ≥ 100 mg/dL (≥ 5.55 mmol/L) or consuming antiglycemic agents.

IDF: MetS was defined as if had central obesity (waist circumference ≥ 90 cm in men or ≥ 80 cm in women) plus at least two of the following: (1) raised triglycerides > 1.7 mmol/L or using specific treatment for this lipid abnormality; (2) reduced high-density lipoprotein cholesterol < 1.03 mmol/L in men or < 1.29 mmol/L in women or using specific treatment for this lipid abnormality; (3) raised blood pressure (systolic ≥ 130 mmHg or diastolic ≥ 85 mmHg or using antihypertensive drugs); and (4) raised fasting plasma glucose > 5.6 mmol/L or previously diagnosed type 2 diabetes.

NCEP ATPIII criteria: MetS was defined if had at least three of the following: (1) waist circumference ≥ 90 cm in men, or ≥ 80 cm in women; (2) systolic blood pressure ≥ 130 mmHg, and/or diastolic blood pressure ≥ 85 mmHg, or using antihypertensive drug treatment; (3) fasting glucose > 100 mg/dL, or using drug treatment for elevated glucose; (4) triglyceride > 150 mg/dL, or using drug treatment for elevated triglycerides; (5) high-density lipoprotein cholesterol < 50 mg/dL in women, or < 40 mg/dL in men, or using drug treatment for reduced high-density lipoprotein cholesterol.

AHA/NHLBI criteria: MetS was defined if 3 out of the following 5 criteria are met, (1) waist circumference ≥ 80 cm, (2) blood pressure > 130/85 mmHg or on antihypertensive medication, (3) fasting plasma glucose > 100 mg/dL or on anti-diabetic medication, (4) fasting triglyceride > 150 mg/dL, (5) high-density lipoprotein < 50 mg/dL or on antihyperlipidemic medications.

2007 ESH-ESC Guidelines: hypertension was defined as systolic blood pressure > 140 mmHg or diastolic blood pressure > 90 mmHg or taking antihypertensive medicines

*Incidence rate in per 100 000 person year is only calculated when the mean year of follow-up is above 1 year.
such as greater pre-pregnancy BMI (8, 9), excessive weight gain (3), unhealthy dietary patterns (3), physical inactivity (3), and a short period of lactation (3, 10). In the Asian population, there are also quite a few at-risk pre-natal maternal characteristics recently added to this pond of evidence, such as family history of diabetes (43), a higher degree of consanguineous marriages (43), higher pre-pregnancy BMI (29, 31, 32, 46), higher total cholesterol quartile at GDM diagnosis during the index pregnancy (47), younger age at delivery (<30 years) (46), and a short period of lactation (<6 months) (33). Post-natal risk such as missing medical assistance in the continuum of GDM care after delivery could be another risk for T2D progression among Asian mothers with a history of GDM (48).

Cardiovascular Disorders

Hypertension

A history of GDM was related to increased risk of hypertension (HTN) after the index pregnancy in some but not all studies. For instance, the US Nurses’ Health Study found an increased risk of postpartum HTN among women with a history of GDM (49). In contrast, a Dutch cohort suggested the risk of developing HTN was mainly significant among women with a history of hypertensive disorders during pregnancy (HDP) rather than GDM (50). Among the three studies identified in our review on GDM and subsequent hypertension risk (28, 30, 38), the Chinese Tianjin GDM prevention program reported a much higher incidence rate of HTN among women diagnosed with HDP and GDM than women with GDM alone (118 vs. 26 per 1000 person-years) (38), which partially agreed with the Dutch cohort.

The mechanisms underlying postpartum HTN in women with GDM remain un-elucidated. Insulin resistance may be a component of the underlying pathophysiology linking GDM with postpartum HTN, with or without HDP (51). As we know, obesity and excessive weight gain during pregnancy are associated with insulin resistance (38), inflammation and oxidation (52), all of which may lead to permanent vascular damage (51) and even irreversible peripheral vascular resistance. Due to the largely inadequate evidence, future research to investigate the role of antenatal and postpartum lifestyle (e.g., dietary patterns, physical activities) in the progression of HTN is warranted in Asians.

Cardiovascular Risks and Cardiovascular Diseases

Emerging evidence has led to the increasing recognition of the association between GDM and cardiovascular (CV) risks and CV events later in life (53). Previous studies in the Western population have identified a higher level of inflammatory (e.g., C-reactive protein) (54), vascular endothelial dysfunction (e.g., intimal medial thickness) (55), and a 2-7 times higher risk of coronary artery calcification or CVD after 12-15 years' follow-up (56–58), among women with a history of GDM. In Asia, five studies reported metabolic syndrome in Asian women with a history of GDM, with an incidence rate ranging from 40 to 90 per 1000 person-years. One Chinese study reported postpartum dyslipidemia (38.5%) among women with a history of GDM (47), while the other Israelite study reported a 30-70% higher risk of developing CV events and CV hospitalization among women with a history of GDM, even after adjusting for pre-eclampsia and maternal obesity at index pregnancy (39).

Thus far, only determinants for postpartum CVD risks and CV events were reported as family history of T2D (59) and postpartum development of T2D (58) in the western population. Even though postpartum CVD determinants among women with GDM have yet to be fully investigated, long-standing exposure to cardio-metabolic risks has been speculated in the GDM-CVD link.

Cancer

GDM was associated with 30-40% increased risks of breast cancer, thyroid cancer, stomach cancer, and liver cancer for all races and ethnicities in a recent meta-analysis (60). As in the Asian population alone, we identified six retrospective cohort studies (Taiwan, South Korea and Israel) using either national insurance or a medical database to investigate the association between GDM and various cancers. All of them reported higher incidences of breast cancer, thyroid cancer, pancreatic cancer, ovarian cancer, lung cancer, and kidney cancer among the Asian female population with a history of GDM after a median of 5-38 years of follow-up than those parous women without such a history. For example, the incidence rate of cancer among Israelite women with a history of GDM was reported in breast (2 per 1000 person year) (37) and ovary (1 per 100 person year) (36), respectively.

It has been well documented that T2D is associated with higher risks of all-cancer incidence (61), especially malignancies in the breast, pancreas, and liver in women (62, 63). Some evidence has alluded to the mitogenic effect while binding to the insulin-like growth factor-I receptor secondary to insulin resistance (64). Furthermore, hyperglycemia itself might promote carcinogenesis via increasing oxidative stress (65, 66). However, data regarding cancer risks associated with GDM are merely gathered in the Western population.

Liver Dysfunction

Liver dysfunction is a common cause of chronic liver disease that affects approximately one in four adults worldwide, which is characterized by liver steatosis (fat deposition), inflammation, and hepatocyte damage (67). Researchers have suggested a link between metabolic risks (i.e., obesity, hyperglycemia, hyperlipidemia, and insulin resistance) and hepatic fatty deposition and non-alcoholic fatty liver disease (NAFLD) in the past decades (68, 69). Notably, women with a history of GDM were found to have raised liver triglyceride (TG) levels, highlighting a potential link between GDM and liver dysfunction (70, 71). Despite the higher prevalence of postpartum liver fat (72), abnormal liver score (73) and even NAFLD (71, 74), such results were mostly gathered from the Western population. There is one study from South Asia (India) reported a 2.11-fold higher odds of NAFLD among women with GDM, compared with women without GDM. The researchers suggested that postpartum medical conditions such as overweight/obesity, metabolic syndrome, and prediabetes were
risk factors for developing NAFLD, during a median of 16 months’ follow-up after delivery (40).

**Adverse Health Outcomes of Offspring Born From Pregnancies Complicated by GDM**

**Overview**

A body of evidence has implied that specific developmental programming in offspring is influenced by maternal hyperglycemia; in particular, epigenetic modification may be the key underlying mechanism (75, 76). Our review identified forty-two studies conducted on Native Asians (Table 2) and eight studies conducted on Asian immigrants (Supplementary Table 7) with up to 18 years’ follow-up, all of which were within the research scope of adverse health outcomes among offspring born to mothers with GDM. Offspring health outcomes, including fetal growth and neonatal anthropometric measures, were reported in Native Asians and Asian migrants, whereas offspring health outcomes, including congenital anomalies, neuro-cognitive function, and cardio-metabolic phenotypes, were only reported in Native Asians (Figure 4). None of these studies investigated risk factors underlying maternal GDM and the development of offspring health outcomes. Among 50 included studies in this topic, fourteen (28%) were assessed low in risk of bias, while the rest 72% were assessed either high or very high in risk of bias.

**GDM and Fetal Growth**

*In-utero* over nourishment can lead to fetal overgrowth, and such influence may predispose the offspring to obesity and T2D later in life if there is an obesogenic environment (84). A cohort in India reported an association between GDM and antenatal fetal growth at mid-late trimester (85). In this prospective cohort, fetuses of women with GDM had a thicker anterior abdominal wall while smaller femur length and biparietal diameter than fetuses of women without GDM. The researcher referred to this as “the thin-fat-phenotype” which represented a predisposition to T2D at birth (85).

Among Asian immigrants, one Norwegian study found that fetuses exposed to maternal GDM tended to be smaller in fetal weight at 24 weeks of gestation but thereafter grew faster until delivery, compared with fetuses not exposed to maternal with GDM (86). This trend was more prominent in South Asian women (86).

**GDM and Neonatal Outcomes**

**Anthropometric Outcome At Birth**

It is well-accepted that GDM is related to increased risk for macrosomia and large for gestational age (LGA) (6). We identified 14 papers that focused on this topic, with sample sizes ranging from 72 to 11 999 neonates. Among them, the majority reported consistent findings on either higher prevalence rates (11% to 40%) or higher risk ratios (2.0-2.7 times) of macrosomia or LGA among neonates born to GDM mothers, compared with their non-GDM counterparts, despite a couple reported otherwise. Interestingly, one study specifically looked at different combinations of glycemic abnormalities (fasting, 1-hour, and 2-hour glycemic levels) with macrosomia (77). The researchers found that women with three abnormal OGTT glycemic values had a much higher macrosomia rate in their offspring than those with two or one abnormal glycemic value (77). Such results—to some extent—suggested there might be remarkable neonatal outcomes specific to different GDM phenotypes (77).

Four studies reported neonatal birth size in Asian migrants equivocally. The US studies showed no differences in macrosomia rate between neonates born to NHW and Asian women with GDM (87, 88). In contrast, compared with the NHW counterparts, the Dutch study showed a lower macrosomia rate in offspring born to West Asian migrants (Turkish) (89) (18.6% vs. 22.6% [NHW]), while the Canadian study found that newborns born to South Asian female migrants had a greater skinfold thickness (11.7 vs 10.6 mm [NHW]; p=0.0001) (90).

**Neonatal Health Outcomes**

Eight papers reporting other neonatal conditions were identified in our review, ranging from 72 to 10 543 in sample size. Neonatal disorders were listed as hypoglycemia, low Apgar score, hyperbilirubinemia/jaundice, polycythemia and respiratory distress syndrome. All studies consistently reported that neonates born to women with GDM were more susceptible to hypoglycemia, hyperbilirubinemia, respiratory distress syndrome and low Apgar score (<7 at 5 minutes), compared with those born to women without GDM.

**Congenital Diseases**

A total number of six studies reported findings on this topic, only half of which had specified the type of malformation as either congenital heart disease or congenital anomalies of the kidney and urinary tract (CAKUT). In general, there were no differences in congenital heart disease and CAKUT, especially more evident in male neonates (79). Despite the unclear pathophysiological mechanism, it has been speculated that serial maternal antenatal characteristics could affect embryonic development during the first trimester, such as pre-existing diseases prior to pregnancy, overweight and obesity, and excessive weight gain during pregnancy (79, 91, 92).

**Neuro-Cognitive Structure and Function**

There is one case-control study investigated brain function in pre-term infants born to mother with GDM. In the first 33 days after delivery, the researchers used MRI image and discovered that infants born to mother with GDM tended to have multiple reduced fractional anisotropy in the brain, reflecting a microstructural white matter abnormalities compared with the infants born to mother without GDM (80).

**GDM and Childhood Outcomes**

Twenty studies on this topic were identified, with nearly half reported in China (n=8), then followed by India (n=4), Israel (n=3), Hong Kong (n=3), Pakistan (n=1), and Sri Lanka (n=1). Childhood outcomes spanned several traits and conditions,
including adiposity and cardiometabolic outcomes, cognitive function, endocrinological and ophthalmological morbidity.

**Anthropometry, Blood Pressure and Cardiometabolic Outcomes**

The majority of studies (17/20, 85.0%) reported consistent findings on long-term outcomes like childhood adiposity and cardiometabolic risks. Overall, offspring born to women with GDM had higher BMI z-score, higher systolic blood pressure and diastolic blood pressure, higher childhood overweight and obesity rates, higher lipid profile levels, and higher insulin and insulin resistance levels, than those born to women without GDM. These studies involved small (n=164) to large (n=27 157) sample sizes of offspring with an average follow-up of 1-18 years among different ethnicities (Chinese, Indians, Sri Lankans and Israelite Jews).

In terms of cardiac function, we included one Pakistani study (93) and one Indian study (81) with small sample sizes of 136 and 236. Compared with their counterparts, offspring born to women with GDM had higher Carotid Intima-Media Thickness (cIMT), cardiac output and stroke volume, decreased mitral E/A ratio, and total peripheral resistance in early childhood and early adolescence, respectively.

Among Asian immigrants, two studies in the UK (94, 95) and one study in the US (96) with sample sizes ranging from 382 to 6 060 reported a consistent association between GDM and childhood obesity across all races and ethnic groups. The magnitude in such association between NHW women and Asian female immigrants was similar.

**Neuro-Cognitive Outcomes**

Hyperglycemia during pregnancy may affect fetal neurodevelopment and leave a significant impact on offspring cognition (97). Only one Indian study reported neurocognitive outcomes in the offspring at a mean 9.7 years of age (82). Children born to women with GDM had higher learning, long-term retrieval and storage, and better verbal ability than children born to women without GDM. The authors propose that the finding may be confounded by the strong correlation between GDM and higher social-economic status among this cohort (82).

**Endocrinological and Ophthalmological Outcomes**

Other childhood outcomes related to GDM include endocrine and ophthalmic morbidities. In two large-scale Israeli cohort studies where young adults (≤ 18 years) with a history of small-than-gestational age (SGA) conditions were recruited. One study showed no difference in the incidence of endocrine morbidity between young adults born to women with and without GDM (83). In contrast, the other study observed a higher prevalence of offspring ophthalmic inflammation (0.74% vs. 0.60%) and a 60% higher risk in ophthalmic-related hospitalization among young adults born to women with GDM and treated with medication (metformin, insulin) (78).

**DISCUSSION AND FUTURE DIRECTION**

Our review reinforces that, in general, Asians are at the highest risk of developing GDM and for subsequent progression to T2D among all populations. Yet, data among the Asian population on long-term health implications of GDM on women and offspring remain limited and are less in-depth than the Western population. In addition, studies in identifying attributable risk factors that may inform preventive strategies of long-term adverse health outcomes among women and their offspring are less comprehensive in Asians than in the Western population. Methodologically, inferences from existing published data are hindered by considerable heterogeneity in study designs, a high risk of bias (Supplementary Tables 1, 2), and standardized protocols for defining studies of Asians.

In order to address such critical knowledge gaps, future endeavors in the following aspects may be warranted to dissect...
### TABLE 2 | Summary of GDM-related offspring health outcomes in Asians.

| Offspring outcomes | Country | No | PMID or Doi | Author | Year | Study design | Mean or range of follow-up | Total offspring number and outcomes definition | Baseline maternal age, & offspring age | Multiple variable adjustment | Effect size (referencing to non-GDM mothers) |
|--------------------|---------|----|-------------|--------|------|--------------|-----------------------------|-----------------------------------------------|---------------------------------------------|-------------------------------------------|--------------------------------------------|
| **Fetal outcomes** | **Anthropometry** |  |  |  |  |  |  |  |  |  |  |
| India | 1 | 27913848 | Venkataraman et al. | 2016 | Prospective cohort | during pregnancy | 153 fetus with GDM mothers, 179 fetus with non-GDM mothers | Dobut: 28.6 years, Fetus: 20 wks GA, 28-32 wks GA | Maternal age, BMI, parity, gestational weight gain, fetal sex and gestational age | Multiple variable adjustment | Fetuses born to GDM mothers had significantly thicker anterior abdominal wall thickness (20 weeks: 0.26 mm, 0.15-0.37, p<0.0001; 28-32 weeks: 0.48, 0.30-0.65, p<0.0001). |

| Neonatal outcomes |  |  |  |  |  |  |  |  |  |  |  |
| China | 2 | 33407256 | Hu et al. | 2021 | Prospective cohort | at birth | 205 newborns born to GDM mothers, 740 newborns born to non-GDM mothers | Mom: 31.3 years, Offspring: newborn | Age of infants at each measurement, pre-pregnancy BMI, maternal age, parity and gestational age | Crude model | Offspring born to mothers with GDM had higher weight-for-length z-score (WFLZ) [b: 0.26 SD units (95% CI: 0.13-0.40)] across infancy than those of mothers without GDM. |
| China | 3 | 29886780 | Yan et al. | 2020 | Prospective cohort | at birth | 205 newborns born to GDM mothers, 740 newborns born to non-GDM mothers | Mom: 30.5 years, Offspring: newborn | Maternal age, education, average monthly household income, postpartum BMI, parity, passive smoking, family history of diabetes, iron supplementation, multivitamin supplementation, gestational dietary intake, and alcohol use. | Crude model | Infants born to GDM mother had higher risk of macrosomia (RR: 2.11, 95% CI: 1.16-3.83). |
| China | 4 | 31731641 | Cheng et al. | 2019 | Prospective cohort | at birth | 13 newborns born to GDM mothers (n=97); 51 born to non-GDM mothers (n=853) | Mom: did not mention, Offspring: newborn | Maternal age, family history of diabetes, height, parity, nationality, GA at delivery, child gender, smoking or alcohol use before or during pregnancy, intervention for GDM. | Crude model | Infants born to GDM mother had higher risk of macrosomia (OR: 2.70, 95% CI: 2.15-3.40) and LGA (OR: 2.57, 95% CI: 2.05-3.21). |
| China | 5 | 31271909 | Yang et al. | 2019 | Prospective cohort | at birth | 238 newborns born to GDM mothers (n=1495); 1553 born to non-GDM mothers (n=1876). | Mom: 28.5 years, Offspring: newborn | Maternal age, education, average monthly household income, postpartum BMI, parity, passive smoking, family history of diabetes, iron supplementation, multivitamin supplementation, gestational dietary intake, and alcohol use. | Crude model | Based on the OGTT results, women had three abnormal glucose values had more macrosomia (46/406; 11.3%) than women had two (51/939; 5.4%) or one (81/1876; 4.3%) abnormal glucose values (p<0.001). |
| China | 6 | 30412096 | Ding et al. | 2018 | Retrospective cohort study | at birth | 178 newborns born to GDM mothers (n=3221) | Mom: 32.7 years, Offspring: newborn | Maternal age and gestational weeks. No difference in macrosomia and LGA between infants born to GDM and non-GDM mothers. Infants born to obese GDM mothers had higher macrosomia (p=0.001) and LGA (p<0.001) prevalence than non-obese GDM mothers. | Crude model | Infants born to GDM mothers had an increased risk of macrosomia (OR: 2.42, 95% CI: 2.26-2.59). |
| China | 7 | 27806670 | Wang et al. | 2017 | Retrospective cohort study | at birth | 447 newborns born to GDM mothers (n=939); 7975 born to non-GDM mothers (n=12900). | Mom: did not mention, Offspring: newborn | Maternal age and gestational weeks. No difference in macrosomia and LGA between infants born to GDM and non-GDM mothers. Infants born to obese GDM mothers had higher macrosomia (p=0.001) and LGA (p<0.001) prevalence than non-obese GDM mothers. | Crude model | GDM mothers had higher rate of LGA infants (14% vs. 10.4%, p=0.005), compared with non-GDM mothers. |
| China | 8 | 26496961 | Zhao et al. | 2015 | Prospective cohort | 5-10 years | 1501 newborns born to GDM mothers (n=1086); 183 born to non-GDM mothers (n=1756). | Mom: 29.8 years, Offspring: newborn | Maternal age and gestational weeks. No difference in macrosomia and LGA between infants born to GDM and non-GDM mothers. Infants born to obese GDM mothers had higher macrosomia (p=0.001) and LGA (p<0.001) prevalence than non-obese GDM mothers. | Crude model | GDM mothers had higher rate of LGA infants (14% vs. 10.4%, p=0.005), compared with non-GDM mothers. |
| China | 9 | 26401753 | Wang et al. | 2015 | Prospective cohort | at birth | 49 newborns born to GDM mothers (n=887; 114 obese vs. 473 non-obese); 33 born to non-GDM mothers | Mom: 30.2 years, Offspring: newborn | Maternal age and gestational weeks. No difference in macrosomia and LGA between infants born to GDM and non-GDM mothers. Infants born to obese GDM mothers had higher macrosomia (p=0.001) and LGA (p<0.001) prevalence than non-obese GDM mothers. | Crude model | GDM mothers had higher rate of LGA infants (14% vs. 10.4%, p=0.005), compared with non-GDM mothers. |

(Continued)
| Offspring outcomes | Country | No | PMID or Doi | Author Year | Study design | Mean or range of follow-up | Total offspring number and outcomes definition | Baseline maternal age, & offspring age | Multiple variable adjustment | Effect size (referencing to non-GDM mothers) |
|--------------------|---------|----|-------------|-------------|--------------|---------------------------|-----------------------------------------------|-------------------------------------|-------------------------------|-----------------------------------------------|
|                    |         |    |             |             |              |                           |                                               |                                     |                               |                                               |
|                    | Bangladesh | 11 | 26376766  | Chen et al. 2015 | Prospective cohort study | 0-478 years | LGA: n=182 born to GDM mothers (n=587: 144 obese vs. 433 non-obese); n=136 born to non-GDM mothers (n=478) | LGA: n=97 born to GDM mothers (n=1049) | Multiple variable adjustment | Compared with normal weight GDM mothers, Infants born to overweight or obese GDM mothers had higher risk of LGA than normal weight GDM mothers (OR: OR 3.8; 95% CI: 2.0-7.0; OB: OR 2.0; 95% CI: 1.2-3.3). Compared with normal GWG mothers with GDM, infants born to GDM mothers with excessive GWG had higher risk of LGA (OR: 3.3; 95% CI: 2.1-5.1). |
|                    | South Korea | 12 | 9314639  | Jang et al. 1997 | Case-control study | 0-25 years | Macrosomia: n=10 born to GDM mothers (n=72); n=2 born to non-GDM mothers (n=12) | Macrosomia: n=9 born to GDM mothers (n=65); n=5 born to non-GDM mothers (n=43) | Crude model | Compared with normal weight GDM mothers, Infants born to overweight or obese GDM mothers had higher risk of macrosomia (13.9% vs. 2.8), compared with those born to non-GDM mothers. Infants born to GDM mothers had significantly higher rates of macrosomia (13.9% vs. 3.3%) and LGA (40% vs. 13.1%), compared with non-GDM mothers. |
|                    | Kuwait | 13 | 30944829  | Groof et al. 2019 | Cross-sectional study | 0-25 years | Macrosomia: n=16 born to GDM mothers (n=109); n=43 born to non-GDM mothers (n=758) | Macrosomia: n=9; with 758 years; 30-34 yrs; 92.4% | Crude model | Compared with normal weight GDM mothers, Infants born to overweight or obese GDM mothers had a higher risk of macrosomia (OR = 2.36; 95% CI: 1.14, 4.89). |
|                    | Israel | 14 | 33236556  | Riskin et al. 2020 | Retrospective cohort study | 0-25 years | Macrosomia: n=50 born to GDM mothers | Macrosomia: n=97 born to GDM mothers (n=1049) | Multiple variable adjustment | Compared with normal weight GDM mothers, Infants born to overweight or obese GDM mothers had a higher risk of macrosomia (OR = 2.36; 95% CI: 1.14, 4.89). |
| Offspring outcomes | Country | No | PMID or Doi         | Author            | Year | Study design                  | Mean or range of follow-up | Total offspring number and outcomes definition | Baseline maternal age, & offspring age | Multiple variable adjustment | Effect size (referring to non-GDM mothers) |
|-------------------|---------|----|---------------------|-------------------|------|-------------------------------|----------------------------|-----------------------------------------------|--------------------------------------|----------------------------------------|-------------------------------------|
| Offspring outcomes | Israel  | 14 | 30326556           | Riskin et al.     | 2020 | Retrospective cohort study    | At birth                   | Macrosomia: n=1318 born to GDM mothers (n=11999); n=867 born to non-GDM mothers (n=118623) | Mean: 30.5 years Offspring: 18 years | Crude model                            | Compared with newborn born to non-GDM mothers, newborn born to GDM mothers had 3.6 odds of hypoglycaemia and 11.1 odds of polycythemia at birth. |
| Offspring outcomes | Malaysia | 16 | 31778255          | Samsuddin et al. | 2020 | Prospective cohort study     | At birth                   | Hypoglycaemia: n=11 born to GDM mothers (n=145); n=7 born to non-GDM mothers (n=962) | Mean: 32.3 years Offspring: newborn | Crude model                            | Infants born to GDM mothers had higher rate of hypoglycaemia (9.2% vs. 1.9%), compared with non-GDM mothers. |
| Offspring outcomes | Saudi Arabia | 17 | 26620797       | Alfaedh et al. | 2015 | Prospective cohort study     | At birth                   | Apgar score <7 at 5 minutes: n=23 born to GDM mothers (n=292); n=3 born to non-GDM mothers (n=281) | Mean: 32.3 years Offspring: newborn | Crude model                            | Infants born to GDM mothers had higher risk of neonatal low Apgar score (OR: 5.55; 95% CI: 1.58-19.48) and hypoglycaemia (OR: 9.35; 95% CI: 2.79-31.29). |
| Offspring outcomes | Thailand | 18 | 26111427          | Luengmettakul et al. | 2015 | Retrospective cohort study    | At birth                   | Hypoglycaemia: n=25 born to GDM mothers (n=487); n=2 born to non-GDM mothers (n=345) | Mean: 32.6 years Offspring: newborn | Crude model                            | Infants born to GDM mothers had a higher risk of hypoglycaemia (OR: 12.3; P < 0.0001) and neonatal hyperbilirubinemia (OR: 1.9; P = 0.013). |
| Offspring outcomes | Thailand | 19 | 24372900          | Youngwanichsettha et al. | 2013 | Prospective cohort study     | At birth                   | Hypoglycaemia: n=50 born to GDM mothers (n=118). | Mean: 32.6 years Crude model | The incidence of neonatal hypoglycaemia was 42.4% among women with a history of GDM. | Continued |
| Offspring outcomes | Country | No | PMID or Doi | Author | Year | Study design | Mean or range of follow-up | Total offspring number and outcomes definition | Baseline maternal age,& off-spring age | Multiple variable adjustment | Effect size (referencing to non-GDM mothers) |
|--------------------|---------|----|-------------|--------|------|--------------|---------------------------|-----------------------------------------------|---------------------------------|---------------------------------|-------------------------------------------|
| India              | 20      | 24944938 | Mahalakshmi et al. | 2014 | Retrospective study | Offspring: newborn at birth | Hypoglycaemia: n=22 born to GDM mothers (n=174). | Mom: 29 years | Offspring: newborn | The incidence of neonatal hypoglycaemia was 12.6% among women with a history of GDM |
| Bangladesh         | 11      | http://doi.org/10.3329/jom.v13i2.12749 | Mannan et al. | 2012 | Cross-sectional study | Hyperbilirubinemia: n=60 born to GDM mothers (n=72); n=6 born to non-GDM mothers (n=72); Respiratory distress syndrome: n=8 born to GDM mothers (n=72); n=3 born to non-GDM mothers (n=72). | Mom: 15-25 yrs: 69.5%; 26-35 yrs: 23.6%; 36-45 yrs: 6.9%. Offspring: newborn | Crude model | More babies also suffered from neonatal jaundice (22.2% vs 8.4%, p<0.05) and respiratory distress syndrome (11.1% vs 4.17%, p<0.05) in GDM groups than non-GDM groups. |
| Turkey             | 21      | 322558417 | Vijay et al. | 2020 | Case-control At birth | Vitamin D deficiency (serum values < 20ng/ml): 30 infants born to GDM mothers (n=30); 13 infants born to non-GDM mothers (n=30). | Mom: 30 years old. | Crude model | The mean value of Vitamin D levels in GDM babies was 8.47ng/ml and was 19.51ng/ml in the control (p value <0.001). |
| China              | 6       | 30412096 | Ding et al. | 2018 | Retrospective cohort study | Fetal malformations did not specify: n=33 born to GDM mothers (n=3221); 11 born to non-GDM mothers (n=3221). | Mom: 32.7 years Old. | Crude model | Female malformation rate born to GDM mothers was 1.02%. |
| Turkey             | 22      | DOI:10.5262/tndt.2017.1002.05 | Soylu et al. | 2017 | Case-control study 0-18 years | 21 born to GDM mothers, 259 born to non-GDM mothers CAKUT: n=14 for GDM newborns: n=126 for non-GDM newborns | Mom: Did not mention Offspring: Newborn | Crude model | OAKUT had 10% children born to GDM mothers and the controls only had 5% children born to GDM mothers. However, it is not statistically significant. |
| Taiwan             | 23      | 26844492 | Tain et al. | 2016 | Case-control study | 10543 born to GDM mothers, 1591179 born to non-GDM mothers. Among them: Congenital anomalies of kidney and urinary tract (CAKUT): n=11 born to GDM mothers; n=0 born to non-GDM mothers; Musculoskeletal system anomalies: n=38 born to GDM | Mom: Did not mention Offspring: newborn | Crude model | Infants born to GDM mothers had higher risks of OAKUT (OR 2.22; 95% CI: 1.06-4.67), and also higher prevalence of musculoskeletal system (0.32% vs. 0.17%, p=0.001), eye and face (0.28% vs. 0.17%, p=0.001), heart and circulatory system (0.27% vs. 0.10%, p=0.001) and genitourinary system (0.19% vs. 0.07%, p<0.001), compared those born to non-GDM mothers. |
| Offspring outcomes | Country | No. | PMID or Doi | Author | Year | Study design | Mean or range of follow-up | Total offspring number and outcomes definition | Baseline maternal age & offspring age | Multiple variable adjustment | Effect size (referencing to non-GDM mothers) |
|--------------------|---------|-----|-------------|--------|------|--------------|--------------------------|---------------------------------------------|---------------------------------|----------------------------------|-----------------------------------------------|
|                    |         |     |             |        |      |              |                          |                                                              |                                 |                                  |                                 |
| **Multiple variable adjustment** |         |     |             |        |      |              |                          |                                                              |                                 |                                  |                                 |
| 1. Anthropometry, Blood | China | 26 | 33633685 | Du et al. | 2021 | Prospective cohort | 1 year old | Maternal age, family history of diabetes, parity, gestational weight gain, pre-pregnancy BMI, maternal gestational hypertension, GA, birth weight, birth length, mode of delivery, parental Maternal GDM was found to be independently and significantly associated with overweight or obesity in 1-year aged female offspring only (OR 1.61, 95% CI 1.09–2.37, p < 0.05). |
| 2. Neuro-Cognitive Structure and Function | China | 25 | 33196602 | Xuan et al. | 2020 | Case-control | First 33-day after delivery | Fractional anisotropy was significantly decreased in the splenium of corpus callosum, posterior limb of internal capsule, thalamus in infants born to GDM mothers, reflecting microstructural white matter abnormalities in the GDM group. |
| 3. Anthropometry, Blood | China | 24 | 26071138 | Liu et al. | 2015 | Retrospective cohort study | 6 months | Congenital heart disease: n=206 born to GDM mothers (n=3060); n=17371 born to non-GDM mothers (n=87736). |
| 4. Neuro-Cognitive Structure and Function | Bangladesh | 11 | http://doi.org/10.3329/jom.v13i2.12749 | Mannan et al. | 2012 | Cross-sectional study | at birth | Congenital anomalies (did not specify): n=9 born to GDM mothers (n=174); n=2 born to non-GDM mothers. |
| 5. Anthropometry, Blood | India | 20 | 24944938 | Mahalakshmi et al. | 2014 | Retrospective cohort study | at birth | Congenital anomalies (did not specify): n=9 born to GDM mothers (n=174); n=2 born to non-GDM mothers. |
| 6. Anthropometry, Blood | India | 20 | 24944938 | Mahalakshmi et al. | 2014 | Retrospective cohort study | at birth | Congenital anomalies (did not specify): n=9 born to GDM mothers (n=174); n=2 born to non-GDM mothers. |
| 7. Anthropometry, Blood | Bangladesh | 11 | http://doi.org/10.3329/jom.v13i2.12749 | Mannan et al. | 2012 | Cross-sectional study | at birth | Congenital anomalies (did not specify): n=9 born to GDM mothers (n=174); n=2 born to non-GDM mothers. |
| 8. Anthropometry, Blood | India | 20 | 24944938 | Mahalakshmi et al. | 2014 | Retrospective cohort study | at birth | Congenital anomalies (did not specify): n=9 born to GDM mothers (n=174); n=2 born to non-GDM mothers. |
| 9. Anthropometry, Blood | Bangladesh | 11 | http://doi.org/10.3329/jom.v13i2.12749 | Mannan et al. | 2012 | Cross-sectional study | at birth | Congenital anomalies (did not specify): n=9 born to GDM mothers (n=174); n=2 born to non-GDM mothers. |
| **Multiple variable adjustment** |         |     |             |        |      |              |                          |                                                              |                                 |                                  |                                 |
| 1. Anthropometry, Blood | China | 26 | 33633685 | Du et al. | 2021 | Prospective cohort | 1 year old | Maternal age, family history of diabetes, parity, gestational weight gain, pre-pregnancy BMI, maternal gestational hypertension, GA, birth weight, birth length, mode of delivery, parental Maternal GDM was found to be independently and significantly associated with overweight or obesity in 1-year aged female offspring only (OR 1.61, 95% CI 1.09–2.37, p < 0.05). |
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| 3. Anthropometry, Blood | China | 24 | 26071138 | Liu et al. | 2015 | Retrospective cohort study | 6 months | Congenital heart disease: n=206 born to GDM mothers (n=3060); n=17371 born to non-GDM mothers (n=87736). |
| 4. Neuro-Cognitive Structure and Function | Bangladesh | 11 | http://doi.org/10.3329/jom.v13i2.12749 | Mannan et al. | 2012 | Cross-sectional study | at birth | Congenital anomalies (did not specify): n=9 born to GDM mothers (n=174); n=2 born to non-GDM mothers. |
| 5. Anthropometry, Blood | India | 20 | 24944938 | Mahalakshmi et al. | 2014 | Retrospective cohort study | at birth | Congenital anomalies (did not specify): n=9 born to GDM mothers (n=174); n=2 born to non-GDM mothers. |
| 6. Anthropometry, Blood | Bangladesh | 11 | http://doi.org/10.3329/jom.v13i2.12749 | Mannan et al. | 2012 | Cross-sectional study | at birth | Congenital anomalies (did not specify): n=9 born to GDM mothers (n=174); n=2 born to non-GDM mothers. |
| 7. Anthropometry, Blood | India | 20 | 24944938 | Mahalakshmi et al. | 2014 | Retrospective cohort study | at birth | Congenital anomalies (did not specify): n=9 born to GDM mothers (n=174); n=2 born to non-GDM mothers. |
| 8. Anthropometry, Blood | Bangladesh | 11 | http://doi.org/10.3329/jom.v13i2.12749 | Mannan et al. | 2012 | Cross-sectional study | at birth | Congenital anomalies (did not specify): n=9 born to GDM mothers (n=174); n=2 born to non-GDM mothers. |
| 9. Anthropometry, Blood | India | 20 | 24944938 | Mahalakshmi et al. | 2014 | Retrospective cohort study | at birth | Congenital anomalies (did not specify): n=9 born to GDM mothers (n=174); n=2 born to non-GDM mothers. |
| **Multiple variable adjustment** |         |     |             |        |      |              |                          |                                                              |                                 |                                  |                                 |
| 1. Anthropometry, Blood | China | 26 | 33633685 | Du et al. | 2021 | Prospective cohort | 1 year old | Maternal age, family history of diabetes, parity, gestational weight gain, pre-pregnancy BMI, maternal gestational hypertension, GA, birth weight, birth length, mode of delivery, parental Maternal GDM was found to be independently and significantly associated with overweight or obesity in 1-year aged female offspring only (OR 1.61, 95% CI 1.09–2.37, p < 0.05). |
| 2. Neuro-Cognitive Structure and Function | China | 25 | 33196602 | Xuan et al. | 2020 | Case-control | First 33-day after delivery | Fractional anisotropy was significantly decreased in the splenium of corpus callosum, posterior limb of internal capsule, thalamus in infants born to GDM mothers, reflecting microstructural white matter abnormalities in the GDM group. |
| 3. Anthropometry, Blood | China | 24 | 26071138 | Liu et al. | 2015 | Retrospective cohort study | 6 months | Congenital heart disease: n=206 born to GDM mothers (n=3060); n=17371 born to non-GDM mothers (n=87736). |
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| 5. Anthropometry, Blood | India | 20 | 24944938 | Mahalakshmi et al. | 2014 | Retrospective cohort study | at birth | Congenital anomalies (did not specify): n=9 born to GDM mothers (n=174); n=2 born to non-GDM mothers. |
| 6. Anthropometry, Blood | Bangladesh | 11 | http://doi.org/10.3329/jom.v13i2.12749 | Mannan et al. | 2012 | Cross-sectional study | at birth | Congenital anomalies (did not specify): n=9 born to GDM mothers (n=174); n=2 born to non-GDM mothers. |
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| 8. Anthropometry, Blood | Bangladesh | 11 | http://doi.org/10.3329/jom.v13i2.12749 | Mannan et al. | 2012 | Cross-sectional study | at birth | Congenital anomalies (did not specify): n=9 born to GDM mothers (n=174); n=2 born to non-GDM mothers. |
| 9. Anthropometry, Blood | India | 20 | 24944938 | Mahalakshmi et al. | 2014 | Retrospective cohort study | at birth | Congenital anomalies (did not specify): n=9 born to GDM mothers (n=174); n=2 born to non-GDM mothers. |
| Offspring outcomes | Country | No | PMID or Doi | Author Year | Study design | Mean or range of follow-up | Total offspring number and outcomes definition | Baseline maternal age,&offspring age | Multiple variable adjustment | Effect size (referencing to non-GDM mothers) |
|--------------------|---------|----|-------------|-------------|--------------|---------------------------|-----------------------------------------------|---------------------------------|-------------------------------|-----------------------------------------------|
| pressure, and CV risks | 27 | 32861332 | Liang et al, 2020 | Case-control | 6 years old | matched with offspring gender. Case-control | smoking, breastfeeding status, weaning months. 560 infants born to GDM mothers; 554 infants born to non-GDM mothers matched with age and sex-frequency | Mom: 30.0 years Offspring: 6 years old | Children born to GDM mothers had consistently greater BMI z-score and risk of overweight from year 1 to year 6. |
|                   | 28 | 30181654 | Wang et al. 2019 | Prospective cohort | 1-6 years old | 1500 born to GDM mothers, 2565 born to non-GDM mothers N.A. | Maternal age and ppBMI, education, smoking status, infant feeding and total GA. | N.A. | Children born to GDM mothers had consistently greater BMI z-score and risk of overweight from year 1 to year 6. |
|                   | 29 | 28120666 | Zhang et al. 2017 | Cross-sectional study | 1-5 years old | 1263 born to GDM mothers Childhood obesity: n=128 Childhood central obesity: n=126 Childhood hypertension: n=126 | Maternal age and ppBMI, education, smoking status, infant feeding and total GA. | N.A. | Children born to GDM mothers had consistently greater BMI z-score and risk of overweight from year 1 to year 6. |
|                   | 8  | 26496961 | Zhao et al. 2015 | Prospective cohort | 5-10 years old | Childhood overweight: n=177 born to GDM mothers (n=1068); n=221 born to non-GDM mothers (n=1756). Childhood obesity: n=114 born to GDM mothers (n=1068); n=210 born to non-GDM mothers (n=1756). | Maternal ppBMI, child gender, total GA, infant feeding. | N.A. | Children born to GDM mothers had consistently greater BMI z-score and risk of overweight from year 1 to year 6. |
|                   | 30 | 25716565 | Chang et al. 2015 | 6 years | Crude model | Maternal age and ppBMI, education, smoking status, infant feeding and total GA. | Maternal age and ppBMI, education, smoking status, infant feeding and total GA. | N.A. | Children born to GDM mothers had consistently greater BMI z-score and risk of overweight from year 1 to year 6. |
| Offspring outcomes | Country | No | PMID or Doi | Author | Year | Study design | Mean or range of follow-up | Total offspring number and outcomes definition | Baseline maternal age,&offspring age | Multiple variable adjustment | Effect size (referencing to non-GDM mothers) |
|-------------------|---------|----|-------------|--------|------|--------------|---------------------------|-----------------------------------------------|---------------------------------|-----------------------------------|---------------------------------|
|                    |         | 31 | 24689042    | Liu et al. | 2014 | Prospective cohort | at 1 year | 1420 born to GDM mothers, 2573 born to non-GDM mothers. | Mom: 29.2 years | Offspring: birth, 3 months, 6 months, 9 months, 12 months | Crude model | Children born to GDM mothers had higher BMI (15.8 vs. 12.3, p=0.001), higher sum of skinfold (Subscapular skinfold thickness + Triceps skinfold thickness) (8.2 vs. 4.8cm, p=0.03), compared with those born to non-GDM mothers. |
|                    |         | 32 | 22160003    | Andegiorgish et al. | 2012 | Cross-sectional study | N.A. | Childhood overweight: n=15 born to GDM mothers (n=24); n=518 born to non-GDM mothers (n=1527). | Mom: Did not mention | Offspring: 7-11 years & 12-18 years | Paternal obesity and maternal obesity. | Children born to GDM mothers had higher rate of overweight (2.8% vs. 0.9%, p=0.003), compared with those born to non-GDM mothers. Children born to GDM mother had a higher risk of overweight (OR: 2.76; 95% CI: 1.11–6.87). |
|                    |         | 33 | 2977227     | Hui et al. | 2018 | Prospective cohort | Month 3-year 16 | 539 born to GDM mothers, 6758 born to non-GDM mothers N.A. | Mom: ≤24 yrs: 7.3%, 25-34 yrs: 27%, 30-34 yrs: 40%, ≥35 yrs: 26% | Offspring: 3 and 9 months, 2-8 years, 8-16 years | Maternal age and birth place, SES, parental education, presence of PE, maternal smoking and BMI at visit, history of T2D, Child sex, parity and age at visit. | Children born to GDM mothers had a lower BMI z-score during infancy (p=0.13, 95% confidence interval (CI) -0.22, -0.05) but higher BMI z-scores during childhood (0.14, 95% CI 0.03, 0.25) and adolescence (0.25 95% CI 0.11, 0.38). Breastfeeding for the first three months did not modify the association. |
|                    |         | 34 | 28279981    | Tam et al. | 2017 | Prospective cohort | 7 years | Childhood overweight or obesity (BMI≥85th percentile): n=30 born to GDM mothers (n=123); n=121 born to non-GDM mothers (n=803). | Mom: Did not mention | Offspring: 6.9 years | Crude model | Offspring born to GDM mothers had higher rates of abnormal glucose tolerance (4.7% vs. 1.7%; p = 0.04), higher rates of overweight or obesity, greater BMI, higher blood pressure, lower oral disposition index, and a trend toward reduced b-cell function, compared with those born to mothers without GDM. |
|                    |         | 35 | 19047239    | Tam et al. | 2008 | Prospective cohort | 8 years | 63 born to GDM mothers, 101 born to non-GDM mothers | Mom: 28.5 years | Offspring: 7.7 years | Child age and gender. | Children born to GDM mothers had higher SBP (94 vs 88 mm Hg) and DBP (62 vs 57 mm Hg) and lower HDL (1.58 vs 1.71 mmol/L) levels, compared with those born to non-GDM mothers. |
| Offspring outcomes | Country | No | PMID or Doi | Author | Year | Study design | Mean or range of follow-up | Total offspring number and outcomes definition | Baseline maternal age, & offspring age | Multiple variable adjustment | Effect size (referencing to non-GDM mothers) |
|-------------------|---------|----|-------------|--------|------|--------------|----------------------------|-----------------------------------------------|------------------------------------------|-------------------------------|---------------------------------------------|
|                   |         |    |             |        |      |              |                            |                                               |                                          |                               | Children born to GDM mothers had higher insulin level (54.3 vs. 42.5 pmol/L, p=0.02), higher SBP (mean difference: 5.96; 2.10-9.82) and higher insulin resistance (2.0 vs. 1.6, p=0.02) than those born to non-GDM mothers. Children born to GDM mothers had higher cardiac output (0.49, 0.26-0.72), stroke volume 3.98 (2.00, 5.97) and lower total peripheral resistance (-114; -220~9), compared with those born to non-GDM mothers. Children born to GDM mothers had more adiposity and higher SBP and insulin resistance, compared with control children at age 5 years. And such effects were greater at age 9.5 years. GDM remained significantly associated with offspring 17-year BMI (1.17; 0.81, 1.52) and diastolic BP (1.52; 0.56, 2.48). |
|                   |         |    |             |        |      |              |                            |                                               |                                          |                               | Children born to GDM mothers had higher median BMI (17.8 vs 16.1, p<0.001), waist circumference 83 cm vs 59.3 cm, p< 0.001, and triceps skinfold thickness (13.7mm vs 11.2 mm, p< 0.001), and also higher risk of overweight (OR: 2.6, 95% CI 1.4-4.9) and abdominal obesity (OR:2.7, 95% CI 1.1-6.9) at the age of 10-11 years. |
|                   |         |    |             |        |      |              |                            |                                               |                                          |                               | Children born to GDM mothers with medication had a decreased mitral E/A ratio [IQR] = 1.7 [1.6-1.9] and 1.56 [1.4-1.7], respectively, p = 0.02, compared with those born to GDM mothers treated by diet only, and also a higher cIMT (0.48 vs. 0.46, p = 0.03), compared with those born to non-GDM mothers. There was no significant difference in offspring cardiac morphology, myocardial systolic and diastolic function, and macrovascular assessment GDM and non-GDM groups. Children born to GDM mothers had significant higher learning, long-term retrieval/storage (β: 0.45D, 95% CI: 0.01-0.75; p=0.042) and better verbal ability (0.59D, 0.09-0.83; p=0.015). Young adults born to GDM mothers treated by medication had higher risk of offspring ophthalmic related hospitalization (HR: 1.6, 95% CI: 1.1-2.4) compared with non GDM mothers. |

**TABLE 2 | Continued**

| Offspring outcomes | Country | No | PMID or Doi | Author | Year | Study design | Mean or range of follow-up | Total offspring number and outcomes definition | Baseline maternal age, & offspring age | Multiple variable adjustment | Effect size (referencing to non-GDM mothers) |
|-------------------|---------|----|-------------|--------|------|--------------|----------------------------|-----------------------------------------------|------------------------------------------|-------------------------------|---------------------------------------------|
|                   |         |    |             |        |      |              |                            |                                               |                                          |                               | Children born to GDM mothers had higher insulin level (54.3 vs. 42.5 pmol/L, p=0.02), higher SBP (mean difference: 5.96; 2.10-9.82) and higher insulin resistance (2.0 vs. 1.6, p=0.02) than those born to non-GDM mothers. Children born to GDM mothers had higher cardiac output (0.49, 0.26-0.72), stroke volume 3.98 (2.00, 5.97) and lower total peripheral resistance (-114; -220~9), compared with those born to non-GDM mothers. Children born to GDM mothers had more adiposity and higher SBP and insulin resistance, compared with control children at age 5 years. And such effects were greater at age 9.5 years. GDM remained significantly associated with offspring 17-year BMI (1.17; 0.81, 1.52) and diastolic BP (1.52; 0.56, 2.48). |
|                   |         |    |             |        |      |              |                            |                                               |                                          |                               | Children born to GDM mothers had higher median BMI (17.8 vs 16.1, p<0.001), waist circumference 83 cm vs 59.3 cm, p< 0.001, and triceps skinfold thickness (13.7mm vs 11.2 mm, p< 0.001), and also higher risk of overweight (OR: 2.6, 95% CI 1.4-4.9) and abdominal obesity (OR:2.7, 95% CI 1.1-6.9) at the age of 10-11 years. |
|                   |         |    |             |        |      |              |                            |                                               |                                          |                               | Children born to GDM mothers with medication had a decreased mitral E/A ratio [IQR] = 1.7 [1.6-1.9] and 1.56 [1.4-1.7], respectively, p = 0.02, compared with those born to GDM mothers treated by diet only, and also a higher cIMT (0.48 vs. 0.46, p = 0.03), compared with those born to non-GDM mothers. There was no significant difference in offspring cardiac morphology, myocardial systolic and diastolic function, and macrovascular assessment GDM and non-GDM groups. Children born to GDM mothers had significant higher learning, long-term retrieval/storage (β: 0.45D, 95% CI: 0.01-0.75; p=0.042) and better verbal ability (0.59D, 0.09-0.83; p=0.015). Young adults born to GDM mothers treated by medication had higher risk of offspring ophthalmic related hospitalization (HR: 1.6, 95% CI: 1.1-2.4) compared with non GDM mothers. |

**2. Cognitive function**

| Country | No | PMID or Doi | Author | Year | Study design | Mean or range of follow-up | Total offspring number and outcomes definition | Baseline maternal age, & offspring age | Multiple variable adjustment | Effect size (referencing to non-GDM mothers) |
|---------|----|-------------|--------|------|--------------|----------------------------|-----------------------------------------------|------------------------------------------|-------------------------------|---------------------------------------------|
| India   | 41 | 20614102    | Veena et al. | 2010 | Prospective cohort | 9.7 years | 32 born to GDM mothers, 483 born to non-GDM mothers | Mom: 26.0 years Offspring: 9.7 years | Child’s age, sex, gestation, neonatal weight and head circumference, maternal age, parity, BMI, parent’s socio-economic status, education and rural/urban residence. | Crude model | Children born to GDM mothers had higher learning, long-term retrieval/storage (β: 0.45D, 95% CI: 0.01-0.75; p=0.042) and better verbal ability (0.59D, 0.09-0.83; p=0.015). Young adults born to GDM mothers treated by medication had higher risk of offspring ophthalmic related hospitalization (HR: 1.6, 95% CI: 1.1-2.4) compared with non GDM mothers. |

**3. Endocrinological and Ophthalmological morbidity**

| Country | No | PMID or Doi | Author | Year | Study design | Mean or range of follow-up | Total offspring number and outcomes definition | Baseline maternal age, & offspring age | Multiple variable adjustment | Effect size (referencing to non-GDM mothers) |
|---------|----|-------------|--------|------|--------------|----------------------------|-----------------------------------------------|------------------------------------------|-------------------------------|---------------------------------------------|
| Israel  | 15 | 29429074    | Walter et al. | 2019 | Retrospective cohort study | 18 years | 11999 born to GDM mothers, 226623 born to non-GDM mothers | Mom: 30.8 years Offspring: 2-5 years | Child’s age, sex, gestation, neonatal weight and head circumference, maternal age, parity, BMI, parent’s socio-economic status, education and rural/urban residence. | Crude model | Children born to GDM mothers had significant higher learning, long-term retrieval/storage (β: 0.45D, 95% CI: 0.01-0.75; p=0.042) and better verbal ability (0.59D, 0.09-0.83; p=0.015). Young adults born to GDM mothers treated by medication had higher risk of offspring ophthalmic related hospitalization (HR: 1.6, 95% CI: 1.1-2.4) compared with non GDM mothers. |
| Offspring outcomes | Country | No | PMID or Doi | Author            | Year | Study design | Mean or range of follow-up | Total offspring number and outcomes definition | Baseline maternal age, & offspring age | Multiple variable adjustment | Effect size (referencing to non-GDM mothers) |
|-------------------|---------|----|-------------|-------------------|------|--------------|---------------------------|-----------------------------------------------|----------------------------------------|-------------------------------------|------------------------------------------|
|                   | Israel  | 42 | 31117838    | Shorer et al.     | 2019 | Retrospective cohort study | 18 years                  | 9312 SGA infants: 259 born to GDM mothers, 9053 born to non-GDM mothers. Among all SGA offspring: Thyroid disease: n=0 born to GDM mothers; n=8 born to non-GDM mothers. T1D and T2D: n=0 born to GDM mothers; n=7 born to non-GDM mothers. Hypoglycemia: n=1 born to GDM mothers; n=19 born to non-GDM mothers. Childhood obesity: n=1 born to GDM mothers; n=7 born to non-GDM mothers. Parathyroid hormone disease: n=0 born to GDM mothers; n=3 born to non-GDM mothers. Adrenal hormone disease: n=0 born to GDM mothers; n=2 born to non-GDM mothers. | Mom: 28.9 years Offspring: 18 years | Maternal hypertensive disorders, preterm birth, and maternal age | SGA children born to GDM mothers was not associated with higher risk of long-term endocrine morbidity of the offspring (adjusted HR 1.2, 95% confidence interval 0.27–5.00, p=0.82). |

GDM, gestational diabetes mellitus; DM, diabetes mellitus; HC, head circumference; AC, abdomen circumference; FL, femur length; BPD, biparietal diameter; BMI, body mass index; LGA, large for gestational age; OR, odds ratios; OGTT, oral glucose tolerance test; CAKUT, congenital anomalies of the kidney and urinary tract; SD, standard deviation; HR, hazard ratio; BP, blood pressure; cIMT, carotid intima media thickness.
the vicious circle of “diabetes begetting diabetes” and improve the health and well-being of this and future generations.

1. Conducting large scale well-designed cohort studies and/or consortium networks among Asians to investigate risk factors and etiology of GDM. A better understanding of GDM pathogenesis specific to Asian women shall further enhance our knowledge on the unique GDM characteristics among Asian women and develop more targeted and effective intervention approaches to prevent GDM and interrupt the transgenerational diabetic vicious cycle. However, such GDM heterogeneity-specific maternal health outcomes in Asians are still limited in scope, let alone other elements of the potential impact such as genetic factors and fetal sex. Future endeavors to establish parallel prospective pregnancy cohorts—with longitudinal data collection and comprehensive characterization of metabolic profiles through pregnancy in different Asian regions—are warranted to understand biological differences across Asian ethnicities, identify determinants and even develop prediction models for GDM onset and its phenotype-specific transgenerational health outcomes.

2. Conducting prospective cohort studies and/or intervention studies to follow up both GDM women and their offspring following the index pregnancy to identify factors that may mitigate the adverse impact of GDM on both women and their children. With the increasing awareness of the GDM burden and subsequent adverse health outcomes in Asian women and their offspring, a few large-scale ongoing pre-conception and pregnancy trials have focused on lifestyle intervention in Asia, such as Project SARAS in Mumbai (98) and the VINAVAC study in Vietnam (99). However, inferences from these two trials are inconsistent, which might be hindered by participants’ low compliance, including low uptake rate of OGTT, poor quality of data collection (e.g., physical examination, questionnaires administration) during research visits, and not quantitative constituents in the snack or freshly-prepared food given to the intervention group (98, 99). In terms of postpartum trials, substantial evidence in either lifestyle modifications (100) or pharmacological therapies (101–103) gathered from developed countries has shown promising results. However, intervention studies with customized approaches (e.g., diet recommendation, lifestyle modification) according to the Asian population are much fewer in scope than the Western population. Recently, there have been some improvements, including a few postpartum T2D prevention trials conducted in countries like China (100, 104), Singapore (105), Malaysia (106), and India (107), focusing on lifestyle modification, with a sample range between 77 and 1 414 and a length of follow-up up to 10 years. However, most of them are still ongoing, and only two trials reported more significant weight loss, reduction in waist circumference, and improved glucose tolerance during the 6-12 months’ postpartum period (104, 106).

3. Conducting studies of Health Disparities in GDM Care in Asian Populations across countries and continents. Even though developing countries in Asia (e.g., India) have shown increased life expectancy over the past several decades, health inequity is still a severe national issue as progress is uneven within each country (108). Furthermore, not all but a substantial proportion of Asian migrants in Western countries face socio-economical disadvantages such as access to health care and education (109). Among them, women seem to be more affected than men due to their vulnerability (109). Therefore, the fight against GDM and its harm to Asian mothers and children should account for existing health inequity and develop strategies to address health disparities.

4. Health Care System Improvement in Asia. Emerging evidence has pointed out that a portion of GDM cases was indeed overt diabetes that has not been identified before pregnancy, which ultimately drives the risk of maternal and offspring health outcomes even higher (110). For example, collecting information on pre-existing maternal diabetes or overt diabetes identification during early pregnancy in the Asian health care system is critical to screen for and even prevent offspring congenital abnormality or other adverse fetal and neonatal health outcomes. Ideally, GDM rates in the population could be reduced by individual and societal measures designed to promote healthy lifestyle changes, including optimal dietary intake and increased physical activity in the general population, focusing on the health and fitness of women of reproductive age.

DATA AVAILABILITY STATEMENT

The original contributions presented in the study are included in the article/Supplementary Material. Further inquiries can be directed to the corresponding authors.

AUTHOR CONTRIBUTIONS

L-JL contributed to the review’s framework conceptualization, study, design, literature research, data collection, analysis and interpretation, and manuscript write-up; LH contributed to literature search, data collection and summary; DT contributed to data interpretation and manuscript editing; CZ contributed to the review’s framework conceptualization, study design, data interpretation and manuscript editing. All authors contributed to the article and approved the submitted version.

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SUPPLEMENTARY MATERIAL

The Supplementary Material for this article can be found online at: https://www.frontiersin.org/articles/10.3389/fendo.2022.840331/full#supplementary-material

Supplementary Figure 1 | Flow diagram of search strategy and selection of GDM prevalence in the Asian population including Native Asians and Asian migrants.
Supplementary Figure 2 | Flow diagram of search strategy and selection of GDM-related maternal postpartum health outcomes in the Asian population including Native Asians and Asian migrants.

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Supplementary Figure 3 | Flow diagram of search strategy and selection of GDM-related offspring postpartum health outcomes in the Asian population including Native Asians and Asian migrants.

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