

Pregnancy and neonatal outcomes in Indigenous Australians with diabetes in pregnancy

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Abstract

AIM: To perform a systematic review of reported neonatal and pregnancy outcomes of Indigenous Australians with diabetes in pregnancy (DIP).

METHODS: Electronic searches of PubMed and Web of Science were carried out. Articles were selected if they contained original data on DIP outcomes in Indigenous Australians. There were no specific exclusion criteria.

RESULTS: A total of eight articles, predominantly from Queensland and Western Australia were identified once inclusion criteria were applied. Birth data from midwifery registries or paper charts encompassing years 1985-2008 were used. A total of 465591 pregnant women with and without DIP were included in the eight studies, with 1363 being Indigenous women with DIP. Indigenous Australians experienced increased rates of many known adverse outcomes of DIP including: macrosomia, caesarean section, congenital deformities, low birth weight, hypoglycaemia, and neonatal trauma. There were regional differences among Indigenous Australians, particularly regional/remote vs metropolitan populations where the regional/remote data showed worse outcomes. Two of the articles did not note a difference between Aboriginals and Caucasians in the rates of measured adverse outcome. Studies varied significantly in size, measured outcomes, and subsequent analysis.

CONCLUSION: The health disparities between Indigenous Australians and non-Indigenous Australians are further evidenced by poorer outcomes in DIP. This has broader implications for Indigenous health in general.

Key words: Diabetes; Gestational; Hyperglycaemia; Pregnancy; Indigenous; Aboriginal; Torres Strait Islander; Outcomes

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Core tip: A review of all published data in Australia concerning diabetes in pregnancy outcomes in Indigenous Australians was performed. Of the eight articles identified, Indigenous Australians were shown to have higher rates of adverse outcomes compared to the non-Indigenous population. Living in a remote region appeared to increase the risk of an adverse outcome. This article highlights further health disparities between Indigenous and non-Indigenous, but also exposes gaps in regional data.

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INTRODUCTION

It is well documented that diabetes during pregnancy poses multiple risks for the developing foetus as well as adverse outcomes for both mother and newborn^[1-4]. Common adverse pregnancy outcomes include foetal macrosomia, caesarean delivery, shoulder dystocia, congenital malformations, preterm delivery, neonatal hypoglycaemia, respiratory distress and hyperbilirubinaemia^[5-7].

Type 2 diabetes (T2DM) has been reported to be up to four times more prevalent in Indigenous Australians compared to non-Indigenous Australians^[8,9]. Furthermore, T2DM occurs at younger ages and complications occur earlier in addition to being more severe than in non-Indigenous Australians^[10,11]. There are parallels that can be drawn with Indigenous populations in overseas countries, with studies conducted in North America showing that the First Nations people also suffer an increased prevalence of diabetes and are subject to increased adverse outcomes as a result of diabetes during pregnancy, compared to non-Indigenous citizens^[12-14]. The high rates of T2DM in the Indigenous populations is thought to be related to obesity, high fat and carbohydrate dense dietary changes combined with a more sedentary lifestyle compared to the traditional hunter-gatherer lifestyle^[15]. As obesity is a risk factor for developing T2DM it has been hypothesised to be a cause of increased rates of gestational diabetes and pre-existing diabetes in women of childbearing age^[16].

The Indigenous population is spread out across Australia and a large proportion reside in communities located in rural or remote areas^[17] (Figure 1). Australia has two distinct Indigenous populations: Australian Aborigines and Torres Strait Islanders, the combined population estimated to be 669881 at the

2011 census, of which 90% were of sole Australian Aboriginal origin^[18]. Torres Strait Islanders are ethnically distinct from Australian Aborigines as they are primarily of Melanesian descent. They originate from the Torres Strait region, a region consisting of hundreds of islands between the tip of Cape York on the Australian mainland and Papua New Guinea^[19]. The Torres Strait diaspora are scattered all over Australia in present times. Indigenous women living in remote areas of Australia have been shown to be at greater risk for developing T2DM^[20]. This is related to obesity, physical inactivity, to poor food quality, availability and cost, in addition to poor economic disposition and genetic predisposition. Access to, and quality of services provided to rural and remote communities are frequently lacking due to the transient nature of health professionals working in these areas. Moreover, Indigenous women often present late for antenatal care, increasing the risk of an adverse pregnancy outcome.

The aim of this study was to conduct a systematic review of the current literature surrounding pregnancy and neonatal outcomes in DIP experienced by Indigenous Australian women.

MATERIALS AND METHODS

For this systematic review, the PRISMA guidelines for literature search and reporting were adhered to where they were applicable^[21]. PubMed searches were performed using the search terms "Aboriginal", "Torres Strait Islander", "Indigenous", "diabetes", "pregnancy", "gestational" and "Australia" (Figure 2). Relevant combinations of these terms returned around 40 unique articles. A MeSH search was then carried out using the combination of subject headings: "Pregnancy in Diabetics" or "Diabetes, Gestational" and "Australia". This returned a higher yield, with 185 articles identified. The Web of Science database was also searched using each of the initial PubMed search terms, however this did not reveal any further articles of interest. The last search was performed in November 2014. Papers which mentioned diabetes, pregnancy, outcomes or made reference to Indigenous Australians in their titles and abstracts were downloaded for further evaluation. Around 20 articles were identified, which involved Indigenous Australians and DIP. The references of these articles were screened to identify any further publications that may have been missed in the search, however this did not reveal any additional studies. Of the papers that were downloaded, prevalence of DIP was the topic of focus in roughly half of the articles, leaving a total of eight suitable papers focusing specifically on outcomes in Indigenous women with DIP (Figure 2). Inclusion criteria were articles that reported on pregnancy and neonatal outcomes in DIP experienced by Indigenous Australian women. There were no specific exclusion criteria. A quality analysis of each study was also

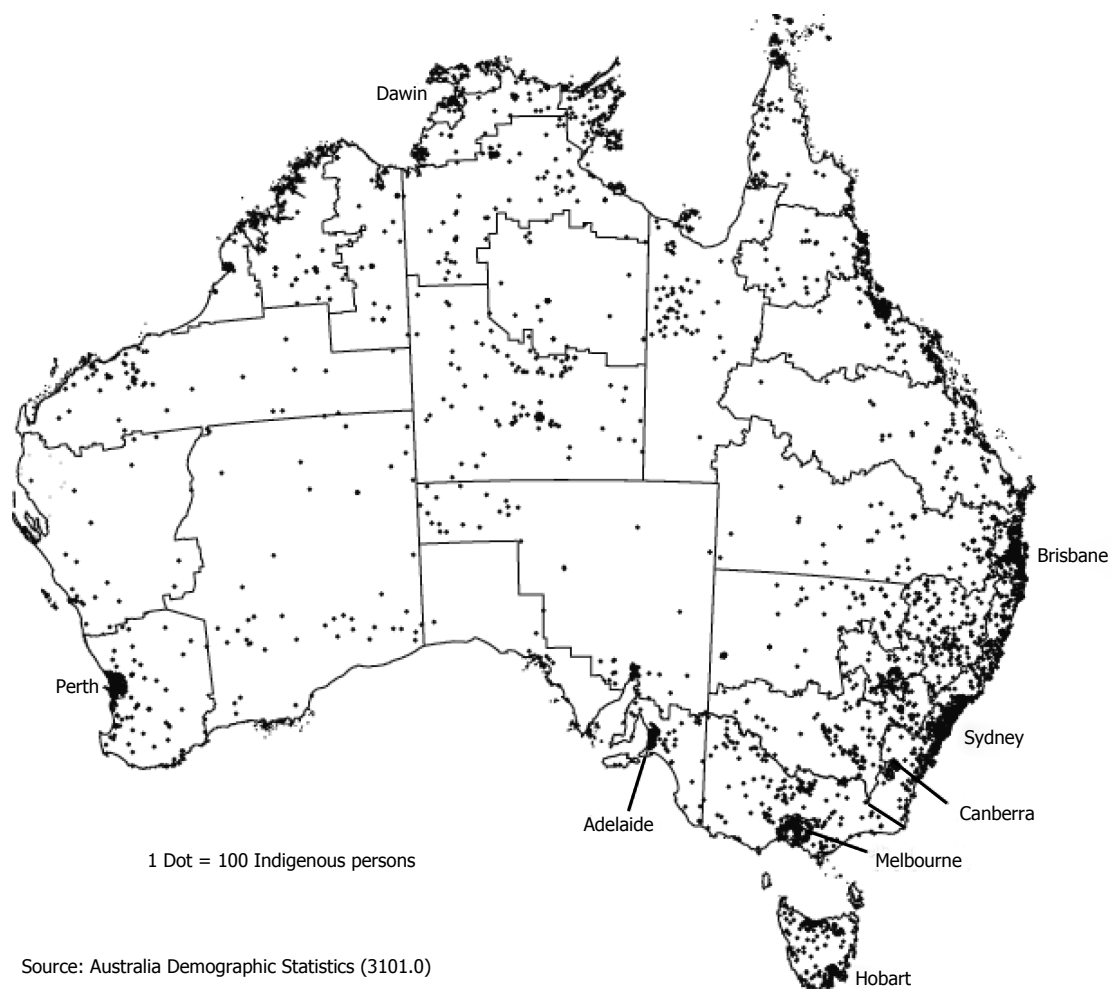


Figure 1 Graphic demonstrating the distribution of Indigenous Australians throughout Australia. Obtained from the Australian Human Rights Commission under Creative Commons^[17].

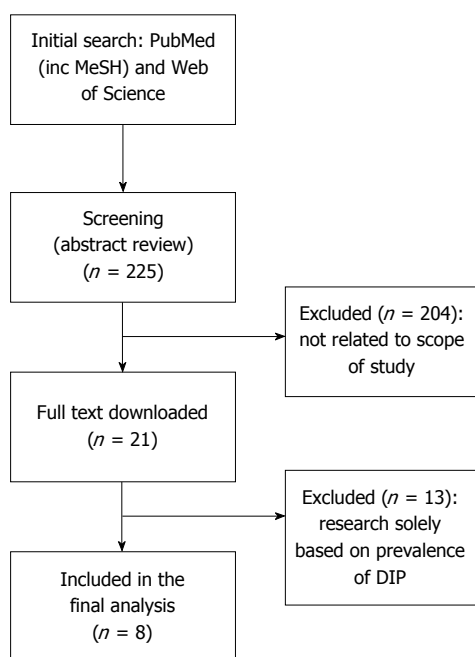


Figure 2 Article selection process for our systematic review. DIP: Diabetes in pregnancy.

performed, outlining merits and limitations of each.

RESULTS

The eight articles gathered from the PubMed database were published between 1985 and 2013. Most were state-wide studies, with three from Queensland (Qld), four from Western Australia (WA) and one from South Australia (SA). All were audits of paper charts or birth registers; in essence, retrospective cohort studies (Table 1). A total of 465591 pregnant women with and without DIP were included in the eight studies, with 1363 being Indigenous women with DIP. Outcomes were usually quoted in terms of rates of incidence, or sometimes where comparison to non-Indigenous was available, risk ratios. The quality of included studies varied (Table 2).

Our search revealed that Indigenous women experienced higher rates of most recordable complications of diabetes than non-Indigenous women, regardless of type 1, 2, or gestational diabetes (GDM). There were two exceptions. Sharpe *et al*^[22] found in their large cohort study in SA that although Aboriginal women had

Table 1 List of included studies, all describing pregnancy and neonatal outcomes in Indigenous Australians with diabetes in pregnancy

Ref.	Year	Title	Study region	Years studied	Total study size	Total women with DIP	Number of Indigenous women with DIP	Outcome measured	Findings
Stanley <i>et al</i> ^[25]	1985	Congenital malformations in infants of mothers with diabetes and epilepsy in Western Australia, 1980-1982	WA	1980-1982	62265	225	52	Congenital anomalies	Relative risk of malformations in Aboriginal DIP - 5.6 compared to 1.9 in non-Aboriginal DIP. Attributable risk however, is low
Bower <i>et al</i> ^[24]	1992	Birth defects in the infants of Aboriginal and non-Aboriginal mothers with diabetes in Western Australia	WA	1980-1984	111019	427	98	Congenital anomalies	Prevalence ratio for birth defects in Aboriginal children is 4.85 for insulin dependent DM and 3.64 for non-insulin dependent DM, compared to 2.08 and 3.64 respectively for non-Aboriginal children
Blair ^[23]	1996	Why do Aboriginal newborns weigh less? Determinants of birthweight for gestation	WA	1980's	1301	672	159	Birth weight	Aboriginal newborns weigh 180 g less than non-Aboriginal (DIP and non-DIP)
Sharpe <i>et al</i> ^[22]	2005	Maternal Diabetes and Congenital Anomalies in South Australia 1986-2000: A Population-Based Cohort Study	SA	1986-2000	282260	7681	432	Congenital anomalies	Congenital anomalies significantly higher in mothers with DIP, relative risk 2.01. No difference with ethnicity
Davis <i>et al</i> ^[28]	2009	Maternal and neonatal outcomes following diabetes in pregnancy in Far North Queensland, Australia	North Queensland	2004	50683 ¹	136	59	C-section, hypoglycaemia, resp distress, abnormal birth weight, term delivery	Compared with non-Indigenous women, Indigenous women had smaller babies, less term deliveries, more severe neonatal hypoglycaemia. Worse outcomes than national and state data
Falhammar <i>et al</i> ^[19]	2010	Maternal and neonatal outcomes in the Torres Strait Islands with a sixfold increase in type 2 diabetes in pregnancy over six years	North Queensland	1999, 2005/2006	454	37	32	C-section, large baby, neonatal trauma, hypoglycaemia	DIP infants heavier (700 g), taller (1.9 cm), more neonatal trauma and hypoglycaemia
Porter <i>et al</i> ^[26]	2011	What is the impact of diabetes for Australian Aboriginal women when pregnant?	WA	2000-2007	81617	5987	531	Birth weight, C-section, stillbirth	Indigenous infants' high birth weight, stillbirth rate = 22/1000 for GDM and 53/1000 for pre-existing DM, compared with 3/100 and 11/1000 for Caucasians
Davis <i>et al</i> ^[29]	2013	A threefold increase in gestational diabetes over two years: Review of screening practices and pregnancy outcomes in Indigenous women of Cape York, Australia	North Queensland	2006, 2008	261	31	31	C-section, birth weight, hypoglycaemia	Higher rates of C-section (66 vs 25%), higher birth weight and increased rate of hypoglycaemia (> 40%) in DIP vs non-DIP Indigenous mothers and babies

¹136 local mothers were compared to diabetic mothers in a national benchmark study ($n = 496$) and to all pregnant data in Queensland 2004 ($n = 50051$).
DIP: Diabetes in pregnancy; C-section: Caesarean section.

Table 2 Quality analysis of included studies, detailing strengths and limitations of each

Ref.	Title	Strengths	Limitations
Stanley <i>et al</i> ^[25]	Congenital malformations in infants of mothers with diabetes and epilepsy in Western Australia, 1980-1982	Large sample size	Retrospective cohort study Only one outcome measure (congenital malformations) Low number of Indigenous women with DIP Time period may not be relevant to modern era
Bower <i>et al</i> ^[24]	Birth defects in the infants of Aboriginal and non-Aboriginal mothers with diabetes in Western Australia	Large sample size	Retrospective cohort study Only one outcome measure (birth defects) Low number of Indigenous women with DIP
Blair ^[23]	Why do Aboriginal newborns weigh less? Determinants of birth weight for gestation	Large sample size	Retrospective cohort study DIP outcomes not main focus of paper
Sharpe <i>et al</i> ^[22]	Maternal Diabetes and Congenital Anomalies in South Australia 1986-2000: A Population-Based Cohort Study	Large sample size	Retrospective cohort study Only one outcome measure (congenital anomalies) Comparison between diabetic and non-diabetic with ethnic background as secondary comparator
Davis <i>et al</i> ^[28]	Maternal and neonatal outcomes following diabetes in pregnancy in Far North Queensland, Australia	Study question aligned with our study question, <i>i.e.</i> , outcomes of DIP in Australian Aboriginal women Large sample size	Retrospective cohort study Low number of Indigenous women with DIP
Falhammar <i>et al</i> ^[19]	Maternal and neonatal outcomes in the Torres Strait Islands with a sixfold increase in type 2 diabetes in pregnancy over six years	Assessment and comparison between two time periods	Retrospective cohort study No comparison with non-Indigenous women Low number of Indigenous women with DIP
Porter <i>et al</i> ^[26]	What is the impact of diabetes for Australian Aboriginal women when pregnant?	Study question mirrors ours Large sample size spanning 7 yr	Retrospective cohort study
Davis <i>et al</i> ^[29]	A threefold increase in gestational diabetes over two years: Review of screening practices and pregnancy outcomes in Indigenous women of Cape York, Australia	Comprehensive analysis of outcomes in Indigenous women with DIP	Retrospective cohort study No comparison with non-Indigenous women Low number of Indigenous women with DIP

DIP: Diabetes in pregnancy.

higher rates of pre-existing diabetes and gestational diabetes than Caucasian women, their rate of birth deformities was only slightly higher compared to the Caucasian group. Blair^[23] found that the increased presence of diabetes, urogenital infections, alcoholism and leprosy contributed to most of the lower birth weight in Indigenous children, but did not observe a higher impact of this compared to non-Indigenous children with similarly affected mothers. There was, however, a discrepancy of 180 g between pure-descent Aboriginal infants and Caucasian infants that was not accounted for by these conditions. Incomplete data on the pathologies and non-medical factors in Aboriginal women were cited as the cause of the discrepancy.

In contrast to the study by Sharpe *et al*^[22], Bower *et al*^[24] discovered in their analysis of midwifery data in WA from 1980-1984 that compared to non-diabetic Aboriginal mothers, birth defects in infants of Aboriginal women with pre-existing DM or gestational diabetes were over three times more common. Similarly, the risk in the Caucasian pre-existing diabetic population was 2.0-3.5 times higher but not increased at all in the gestational diabetes group compared to their non-diabetic counterparts. Thus, if Aboriginal diabetic mothers were compared directly to Caucasian diabetic mothers, there was a 10% increased prevalence of birth defects, which was statistically significant for gestational diabetes ($P = 0.02$) but not for pre-existing diabetes. In a cohort from WA with data from

1980-1982, Stanley *et al*^[25] in their analysis of diabetic and epileptic mothers showed a relative risk of 5.1 (95%CI: 2.6-13.0) for diabetic Aboriginal mothers having children with birth defects, in contrast with 1.7 (95%CI: 0.8-3.5) for Caucasian diabetic vs Caucasian non-diabetic women. There may be some overlap of data in these two similar studies, as the same state-wide database was used in overlapping time periods.

Porter *et al*^[26] in their analysis of the midwifery database in WA from 2000-2007, determined that for the time period studied, Aboriginal infants not only had greater birth weights compared to Caucasian infants when both had mothers with GDM, but when the mother had pre-existing diabetes the Aboriginal infants were smaller. Rates of elective caesarean section in Aboriginal women were 10% lower than for Caucasian women with diabetes, and were even found to be slightly lower than healthy Caucasian women. The other significant adverse outcome was that stillbirths were reported to be extremely high in both Aboriginal women with GDM or pre-existing diabetes (22/1000 and 53/1000 births respectively), while Caucasian women with GDM or pre-existing diabetes only had slightly higher rates (3/1000 and 11/1000 births respectively) compared to their non-diabetic counterparts (2/1000 births). The stillbirth rate in Aboriginal women with DIP was similar or even worse than some of the highest stillbirth rates worldwide in southern Africa and Asia (25 to 35/1000 births)^[27].

Falhammar *et al.*^[19] reported birth data from the Torres Strait Islands, obtaining information from two discrete time periods six years apart. The conclusions drawn were that Torres Strait Islander mothers with DIP experienced higher rates of expected complications compared to Torres Strait Islander mothers without DIP. Hypertension and previous spontaneous abortions were more prevalent, as were caesarean sections, with a fivefold elevation compared to the non-diabetic group in the latter year studied. Infants born to diabetic mothers were also heavier, longer, experienced more neonatal trauma, hypoglycaemia and IV dextrose use.

Two other studies originating from North Queensland examined maternal/neonatal outcomes in Indigenous women. Both included the Torres Strait Islander group in the analysis while recognising the ethnically distinct origin. Davis *et al.*^[28] in 2009 compared local DIP outcomes in Far North Queensland to state-wide and national outcomes. They found that Indigenous women with DIP had smaller babies, less term deliveries and more severe neonatal hypoglycaemia than the non-Indigenous cohort. Importantly, when comparing local and national Indigenous data, locals showed worse outcomes with more premature deliveries and lower APGAR scores. There were no significant differences between the two local populations of Aboriginals and Torres Strait Islanders.

Davis *et al.*^[29] in 2013 examined solely DIP vs non-DIP outcomes in the Indigenous Aboriginal population of Cape York in North Queensland. Analysis was done for two discrete years, 2006 and 2008. DIP women were found to have higher rates of caesarean section, higher birth weight and hypoglycaemia. Outcomes such as mean APGAR score and respiratory distress showed improvement in the latter studied year, after a period of intensive education on GDM screening and management protocols between the two years.

DISCUSSION

While it is widely acknowledged that Indigenous Australians suffer poorer health across a variety of disciplines, this is the first systematic review focusing specifically on outcomes related to hyperglycaemia in pregnancy. The studies identified from our literature search contained much variability in research focus and outcome measurement. Six out of eight studies were in accordance that Indigenous Australian women and their babies are subject to worse outcomes in DIP than their non-Indigenous counterparts, or at least their Indigenous counterparts without DIP. Maternal complications such as delivering prematurely or *via* caesarean section occurred at a higher rate. Neonatal complications including hypoglycaemia, macrosomia or low birth weight, and trauma were also increased to significant levels. The studies were equivocal as to whether there was a higher rate of birth defects compared to non-Indigenous babies. These complications for the infant correspond to poorer

health in adulthood, most importantly an increased risk of developing impaired glucose tolerance, obesity or the metabolic syndrome^[30-34]. For the mother, developing GDM in pregnancy places her at a higher risk of developing T2DM later in life and with subsequent pregnancies^[35]. Furthermore, experiencing a caesarean section may involve undue emotional distress, which is also financially and logistically disruptive as many Indigenous women live in remote communities and are relocated to larger regional centres for delivery. It also exposes them to the range of complications possible from undergoing a surgical procedure and places them at higher risk for future pregnancies. However, one study did show a lower frequency of elective caesarean sections in Indigenous mothers with DIP compared to Caucasian mothers with but also without DIP suggesting that inequality in the health care delivery exists, as discussed below. This may explain some of the differences found in outcomes.

In addition to poorer outcomes compared to non-Indigenous women, there is evidence to suggest that perinatal outcomes for Indigenous women living in rural or remote regions are poorer still, particularly in comparison to those women living in metropolitan areas^[19,28,36]. Two of the three studies performed in northern Queensland had shown that compared to state-wide statistics, people living in the study region experienced worse outcomes. This demonstrates that remoteness is likely to be a compounding factor towards a negative outcome in DIP, for reasons including limited food supply, substandard housing and living conditions, poor access to medical services and financial factors. Cultural barriers for women's non-engagement with mainstream health services in remote areas is multifaceted and incorporates cultural beliefs, conflicting cultural responsibilities, fear, guilt, shame, perceptions of culturally insensitive Western practices in pregnancy care and cultural indifference in health care providers^[37].

This review strikes similarities with Indigenous populations abroad, with a study conducted in Ontario, Canada showing that First Nations women received less antenatal and postpartum care, and that those with DIP were subject to higher birth weights and higher rates of jaundice, neonatal hypoglycaemia and shoulder dystocia^[12]. A separate investigation conducted in Alberta, Canada also confirmed worse perinatal outcomes due to DIP in First Nations women, however found that the prevalence of adverse outcomes varied between different provinces^[13]. Aljohani *et al.*^[14] found that in Manitoba, having gestational diabetes and First Nation status compounded the risk of shoulder dystocia. These similarities to other nations with Indigenous populations allow us to draw on and potentially apply any conclusion obtained from studies performed overseas, and vice-versa.

Early in our search it became apparent that literature focusing on pregnancy and neonatal outcomes in Indigenous Australians with DIP was scarce. Half

Table 3 Indigenous population by state as of 2011

State	Indigenous population	Proportion of total population
New South Wales	208000	2.9%
Victoria	47000	0.9%
Queensland	189000	4.2%
Western Australia	88000	3.8%
South Australia	37000	2.3%
Tasmania	24000	4.7%
Australian Capital Territory	6000	1.7%
Northern Territory	69000	29.8%

Source: Adapted from Australian Bureau of Statistics, Estimates of Aboriginal and Torres Strait Islander Australians, June 2011^[18].

of the studies that were eventually included in our analysis focused on one particular complication of pregnancy and assessed predisposing factors, with DIP and Indigenous status being a variable that may lead to the outcome in question. This limits the perspective on the full spectrum of outcomes of DIP, but also introduces an additional form of bias. Due to the variability of the research focuses and outcomes, detailed statistical analysis and direct comparisons, for instance performing a meta-analysis was not possible.

A point worth noting is that while the Northern Territory (NT) has the highest proportion of Indigenous Australians per capita, comprising 29.8% of the NT population at the 2011 census^[18], there were no studies originating from the NT. In both Queensland and Western Australia Indigenous people make up a much lower 4.8% and 3.2% respectively of the total population, however in some remote regions they make up 50%-90% of the population. These states were the biggest contributors to the data on diabetes in Aboriginal women and their pregnancy outcomes (Table 3). To alleviate the disparity in data output across states, an upcoming NT-based study will analyse many different aspects of DIP in Indigenous Australians^[38].

Due to the limited data available, not all of the known adverse outcomes of pregnancy in a diabetic mother could be fully assessed. Pre-eclampsia is known to occur at a higher rate in mothers with pre-existing diabetes^[5], however has not yet been analysed. Stillbirth, perinatal mortality and transient cardiomyopathy are significant recognised complications^[5,39,40], that require further study. Other complications with lacking data include biochemical derangements with uncertain long-term effects such as low iron stores, hyperbilirubinaemia and hypocalcaemia^[41-43]. With more research on the topic, we will be able to paint a clearer picture of specific outcomes that Indigenous women and their offspring may be more prone to developing. This may in turn be used as endpoints to gauge efficacy of management protocols and allocation of resources.

Diabetes in pregnancy presents itself as one of the many health disparities between Indigenous and non-Indigenous Australians. The rising prevalence of the disease and demonstrated poor outcomes com-

pared to non-Indigenous Australians ensures that this problem will remain topical until it is dealt with effectively. In addition, mothers and their infants who are affected by diabetes suffer consequences, which may not manifest until later in life. The main challenges that face Australian healthcare professionals are twofold: incorporating strict antenatal care into the cultural, spiritual and religious framework of Indigenous Australians, and dealing with the difficulties of delivering evidence-based medical care in rural and remote communities. More research into trends, specific outcomes and data from different regions of Australia will aid in building a clear image of the task at hand, as current data is limited. This will in turn assist in identifying novel intervention strategies to employ, and outcome measures by which to judge the effectiveness of these methods.

COMMENTS

Background

It is well recognised that in general, health outcomes of Indigenous Australians are inferior to those of non-Indigenous Australians. Complications related to having diabetes in pregnancy (DIP) are no exception to this trend. However, no systematic review has previously been performed to summarise the current state of pregnancy and neonatal outcomes experienced by Indigenous Australians with DIP.

Research frontiers

Although Indigenous Australians are known to suffer poorer obstetric outcomes compared to non-Indigenous Australians, less is known of specific outcomes and their relative prevalence.

Innovations and breakthroughs

Previous studies have been small or only investigated few outcomes. This systematic review included in total a large number of pregnant women with and without DIP in eight studies, and many were Indigenous women with DIP. Indigenous Australian mothers with DIP and their offspring experienced increased rates of macrosomia, caesarean section, congenital deformities, stillbirth, low birth weight, hypoglycaemia, and neonatal trauma. There were regional differences among Indigenous Australians, particularly regional/remote vs metropolitan populations, where the regional/remote data showed worse outcomes. However, two of the articles did not note a difference between Indigenous and non-Indigenous in the rates of measured adverse outcome.

Applications

This article summarises the main adverse outcomes that are experienced by Indigenous Australians with DIP. These outcomes can in turn be used as endpoints in assessing the impact of new interventions or policies to improve Indigenous health.

Terminology

Diabetes in pregnancy encompasses all conditions that may result in hyperglycaemia in pregnant women. This includes gestational diabetes mellitus diagnosed during pregnancy, or previously diagnosed type 1 or 2 diabetes mellitus.

Peer-review

The paper appears interesting and very well written paper.

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