Association between maternal mental health-related hospitalisation in the 5 years prior to or during pregnancy and adverse birth outcomes: a population-based retrospective cohort data linkage study in the Northern Territory of Australia

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Summary

Background Mental health conditions prior to or during pregnancy that are not addressed can have adverse consequences for pregnancy and birth outcomes. This study aimed to determine the extent to which women's mental health-related hospitalisation (MHrH) prior to or during pregnancy was associated with a risk of adverse birth outcomes.

Methods We linked the perinatal data register for all births in the Northern Territory, Australia, from the year 1999 to 2017, to hospital admissions records to create a cohort of births to women aged 15–44 years with and without MHrH prior to or during pregnancy. We used Modified Poisson Regression and Latent Class Analysis to assess the association between maternal MHrH and adverse birth outcomes (i.e., stillbirth, preterm birth, low birth weight, and short birth length). We explored a mediation effect of covariates on theoretical causal paths. We calculated the adjusted Population Attributable Fraction (PAF) and Preventive Fractions for the Population (PFP) for valid associations.

Findings From 72,518 births, 70,425 births (36.4% for Aboriginal women) were included in the analysis. The Latent Class Analys identified two classes: high (membership probability of 10.5%) and low adverse birth outcomes. Births to Aboriginal women with MHrH were around two times more likely to be in the class of high adverse birth outcomes. MHrH prior to or during pregnancy increased the risk of all adverse birth outcomes in both populations with risk ranging from 1.19 (95% CI: 1.05, 1.35) to 7.89 (1.17, 53.37). Eight or more antenatal care visits and intrauterine growth restriction mostly played a significant mediation role between maternal MHrH and adverse birth outcomes with mediation effects ranging from 1.04 (1.01, 1.08) to 1.39 (1.14, 1.69). MHrH had a low to high population impact with a PAF ranging from 16.1% (5.1%, 25.7%) to 87.3% (14.3%, 98.1%). Eight or above antenatal care visits avert extra adverse birth outcomes that range from 723 (332–765) stillbirths to 3003 (1972–4434) preterm births.

Interpretation Maternal MHrH is a modifiable risk factor that explained a low to moderate risk of adverse birth outcomes in the Northern Territory. The knowledge highlights the need for the development and implementation of preconception mental health care into routine health services.

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Research in context

Evidence before this study

We searched PubMed for studies published in English that examined a link between maternal mental health-related hospitalisation (MHrH) prior to or during pregnancy and adverse birth outcomes i.e., stillbirth, preterm birth, low birth weight, and short birth length. We used key and MeSH terms *("preconception", OR "pre-pregnancy", OR "prior pregnancy", OR "before pregnancy") AND ("mental disorder" OR "mental illness", OR "substance misuse", OR "depression", OR "anxiety") AND ("Hospitalisation" OR "hospitalis*") AND ("adverse birth outcomes", OR "pregnancy outcome", OR "birthweight", OR "low birth weight", OR, "preterm birth", OR "prematurity" OR "gestational age", OR "stillbirth" OR "fetal death" OR "short birth length" OR "birth length") AND ("Pregnancy", OR "during pregnancy")* to locate appropriate studies. Most of the studies focused on perinatal mental health, child development, and adolescent health outcomes related to maternal mental health disorders during pregnancy. Among the identified studies, we found two related investigations that explored the association between maternal mental health morbidity prior to or during pregnancy and negative birth and infant outcomes. The authors of one of the studies published in the Lancet Psychiatry recommended a mediation analysis to gain a better understanding of pathways explaining the association between maternal MHrH and adverse birth outcomes.

Added value of this study

In this population-based cohort study, we utilised longitudinally linked administrative data spanning a period of 18 years to investigate the relationship between maternal MHrH occurring either 5 years prior to or during pregnancy and associations with adverse birth outcomes. Our research extends previous work by conducting a mediation analysis to reveal potential pathways explaining the link between maternal MHrH and adverse birth outcomes. Moreover, our study uniquely quantifies the population-level impact of all risk factors associated with adverse birth outcomes including MHrH, while also determining the preventive fraction attributed to antenatal care (ANC) - the only variable that appeared to reduce the risk of adverse birth outcomes. Our work also adds further depth by conducting a latent class analysis to identify unobserved variation in the risk of adverse birth outcomes in the population and report on the impact of MHrH. Moreover, our research presents a comparative analysis of exposure and outcomes between non-Aboriginal and Aboriginal populations, shedding light on the significant structural and health service disparities that exist between these two populations.

Implications of all the available evidence

Maternal MHrH is a modifiable factor that is related to an increased risk of adverse birth outcomes. The existing evidence, along with our study, emphasises the need for the development and implementation of preconception mental health care. Given the significant disparities in exposure and outcomes across Aboriginal and non-Aboriginal populations, it is also essential to strengthen culturally safe strategies aimed at closing these gaps.

Introduction

Pregnancy and childbirth can be a time of unparalleled change and hope for most mothers but for some can be overshadowed by complications related to mental conditions during pregnancy and the first postnatal period, known as the perinatal period.[1] Severe mental illness is experienced by mothers in about three in a thousand births.[2] The prevalence of maternal severe mental illness in high-income countries has been increasing in recent years.[3] Mental health conditions during pregnancy do not only occur following conception and most mental illnesses detected during pregnancy were present prior to conception.[1] Parental mental health conditions around the time of conception can significantly increase the short and long-term risks of offspring cardiovascular, metabolic, immune, and neurological morbidities.[4] Maternal mental illness prior to or during the perinatal period has been reported to increase the risk of maternal obstetric complications which can lead to adverse birth and childhood outcomes.[5–8] There is a huge economic burden of perinatal mental illnesses associated with health and social service care for the mother and subsequent childhood morbidity.[9]

WHO has highlighted an urgent need for evidence-based effective community-based interventions to reduce the impacts of perinatal maternal mental disorders.[10] The Mental Health Care in the Perinatal Period—Australian Clinical Practice Guideline states the need for preconception care for women of childbearing age with psychiatric morbidity.[11] Limited studies in Australia have reported on perinatal outcomes associated with severe mental illnesses during pregnancy, with one study specifically focusing on First Nations Australians.[2,12,13] Australia's First Nations communities are made up of Aboriginal and Torres Strait Islander populations, which we interchangeably use Aboriginal

population throughout the paper. No study investigated the burden and risk of maternal mental health-related hospitalisation (MHrH) before or during pregnancy on adverse birth outcomes in the Northern Territory where the burden and consequences are expected to be higher than in the other states. The Northern Territory is a large, remote, and sparsely populated area in Australia with the smallest total population and a greater proportion of Aboriginal people (an estimated total population of 232,605 with just over one quarter (26.3%) being Aboriginal people).[14] Aboriginal Australians are disadvantaged in all parameters of health and welfare, and in the Northern Territory, the Aboriginal population experiences disproportionate levels of poverty, crowded housing, and poor health.[15]

The present study aimed to: (i) explore if and to what extent maternal MHrH prior to or during pregnancy increased the risk of adverse birth outcomes; (ii) investigate the potential pathways that elucidate the link between maternal MHrH and adverse birth outcomes via mediation analysis as suggested in previous study[6]; (iii) to explore any hidden patterns of adverse birth outcomes within a population and determine whether these patterns are correlated with maternal MHrH using Latent Class Analysis (LCA); and (iv) to calculate the public health impacts of maternal MHrH and other prominent factors of adverse birth outcomes in a population using 18 years of perinatal records. Understanding the association between maternal MHrH and adverse birth outcomes has significant clinical and public health implications. Quantifying the risk will inform the allocation of health resources to address the issue. Understanding the mechanisms through which MHrH leads to adverse birth outcomes will enable fine tuning of guidance about optimal preconception care for women experiencing a mental illness.

Methods

Study design and cohort selection

We undertook a population-based retrospective cohort study in the Northern Territory, Australia. The study cohort consisted of births in the Northern Territory to women aged from 15 to 44 years in the years between and including January 1, 1999, and December 30, 2017. We excluded a small number of women who were less than 15 and older than 44 years as adverse birth outcomes related to this age group are potentially biological and are less amenable to intervention.

Outcomes

We chose outcomes that are amenable to support for perinatal women and that align with key priorities of Australian pregnancy care and Healthy Child programme.[16] The adverse birth outcomes of interest were: preterm birth (PTB) (births before 37 completed weeks of gestation), low birth weight (LBW) (birth weight <2500 g), stillbirth (SB) (the birth of an infant of at least 20 weeks' gestation or if gestational age unknown, weighing at least 400 g, which shows no signs of life after birth), and short birth length (SBL) (birth length <47 cm) all recorded as 'yes' or 'no'. These variables were accessed from the Northern Territory Perinatal Data Register, which was established in 1986 as a statutory collection of maternal and perinatal information for all births in the Northern Territory.

Exposure

The exposure for the study was hospitalisation for a mental disorder in the 5 years prior to or during pregnancy. We used the Northern Territory Inpatient Activity collection dataset, an administrative dataset containing detailed information for all admissions to all public hospitals in the Northern Territory, between 1 July 1993 and 31 December 2017. The Hospital admission dataset contained a clinical diagnosis coded using the International Statistical Classification of Disease and Related Health Problems 10th Revision (ICD-10) with up to 50 diagnosis fields. Women were considered exposed if the hospital admission data indicated that they were hospitalised for one or more mental health conditions, as indicated by ICD-9 and 10 codes,[5] listed as primary or within the first ten diagnosis codes. The ICD codes used are presented in Table 1 (Supplementary Information). We first created the following six mutually exclusive broad psychiatric diagnosis categories of maternal MHrH: (i) severe mental illness; (ii) common mental disorders; (iii) personality disorders; (iv) substance misuse; (v) all other adulthood-onset illness; and (vi) all other childhood-onset illness.[17] We then formed three relatively homogeneous psychiatric categories because of small observations in some of the categories: Mental illnesses (merging categories i, ii, iii, v, and vi); substance misuse (category iv); and Both conditions (concomitant occurrence).

To see the effect of exposure on the outcomes at two different exposure times, we created a group of births to women hospitalised for mental health-related disorders 5 years prior to pregnancy or during pregnancy. We used a 5-year look-back as this period prior to pregnancy is reported to be correlated with adverse pregnancy and birth outcomes.[1]

Covariates

We considered pre-specified covariates based on the guideline for antenatal care for women with complex social needs.[16] These include pre-existing conditions (diabetes and hypertension), current obstetric complications (gestational diabetes and pre-eclampsia); morbidity complications during pregnancy (such as anaemia, urinary tract infection (UTI), renal disease), intrauterine growth restriction (IUGR)—determined using the proportion of optimal birth weight (the ratio of observed birth weight to optimal birth weight) for all

pregnancies and is calculated and provided to researchers by the Northern Territory data custodians; smoking, alcohol consumption, and were all recorded as 'yes' and' no'; antenatal care (ANC) services (≤7 visits and >8 visits)[18]; maternal age (five categories: 15–19: 20–24, 25–29, 30–34, 35–44), first child ('yes' or 'no'), parity (0, 1, 2, ≥3), Aboriginal status (Aboriginal and non-Aboriginal population), living in different administrative health districts (Darwin urban, Darwin rural, Katherine, East Arnhem, Barkly, Alice Springs urban, and Alice Springs rural), and history of adversity-related admissions (violence and self-harm) both recorded as 'yes' or 'no'. We accessed the perinatal records, Aboriginal status, and health district variables from the Northern Territory Perinatal Data Register. We accessed history of adversity-related admissions (violence and self-harm) from the Inpatient Activity collection (1993–2017) on the basis of published lists of ICD-9 and 10 diagnosis codes.[5,19] The ICD codes we used are presented in Table 2 (Supplementary Information).

Data source and linkage

The datasets used in this study were sourced from a repository of linked administrative datasets established through the Child and Youth Development Research Partnership (CYDRP)—a collaboration between Menzies School of Health Research and NT Government agencies. The detailed data linkage process has been described and published elsewhere.[20] The first stage data linkage process was carried out by the South Australia (SA)-Northern Territory DataLink using a probabilistic linkage method with a clerical review of uncertain matches.[21] The second stage of linking the separate de-identified data files and preparing a dataset for analysis was done by a research team.

Statistical analysis

We prepared the analysis dataset by linking the Perinatal Data Register to the Inpatient Activity collection where we combined the exposure, outcome, and potential covariates. We checked for data completeness, missingness, multicollinearity and potential misclassification of exposure variable and made appropriate corrections prior to analysis. Missing was identified for maternal smoking and drinking during pregnancy. We used missing indicator rather than multiple imputation as the mothers tend not to disclose their smoking or drinking status likely due to social desirability and the missingness is potentially missing not at random (MNAR) where multiple imputation is not advisable.[22] The exposure, hospitalisation for mental health-related disorders, was assessed for the 5 years prior to and during pregnancy. We calculated the prevalence of women hospitalised for mental illness, substance misuse, and for both types with their 95% confidence intervals (CI). We calculated the cumulative incidence of adverse birth outcomes with their 95% CI.

We first conducted a latent class analysis (LCA) to identify sub-groups (classes) of births with similar patterns of adverse birth outcomes.[23] We conducted stepwise analysis—fitting a one-class model, two-class model, and three-class model. We used both statistical and theoretical interpretability to compare the models. A model with two classes fit the data better than the one- and three-class model as it had low Bayesian Information Criterion (BIC) and Akaike Information Criterion (AIC) as well as better theoretical interpretability.[24,25] We also saved class membership to explore if maternal MHrH and Aboriginal status explain variations in adverse birth outcomes grouped in different latent classes. We then estimated the incidence rate ratio (IRR) of adverse birth outcomes using a Modified Poisson regression comparing women with and without a history of MHrH in the 5 years prior to and during pregnancy adjusting for available confounders.[26] Our analysis, employing a modified Poisson regression, ensures that potential statistical issues such as zero-inflation and variance over-dispersion were considered and adequately addressed. All models used robust standard errors to allow for potential clustering effects in the data. We then explored a potential mediation effect of covariates supposed to be on the causal paths and associated with adverse birth outcomes in an adjusted model using a Logit Model.[27] We conducted a separate analysis for non-Aboriginal and Aboriginal women as a prevalence of MHrH 5 years prior to or during pregnancy, cumulative incidence of adverse birth outcomes, and risk of the exposure on the outcomes differs across the two populations (Tables 3–5 and Figs. 1–4 in Supplementary Information).

We finally calculated potential population level impacts of MHrH and other strong predictors of adverse birth outcomes using adjusted Population Attributable Fraction (aPAF) and Prevented Fraction for the Population (aPFP). The PAF estimates a fraction of ABOs that attributed to maternal MHrH that can then be avoided if public health and clinical interventions are designed to eliminate MHrH.[28,29] We calculated PAF using *punaf* command in Stata 17 by comparing exposure free scenario (zero counterfactual) to the real world scenario (as observed in our adjusted model).[30] aPFP was calculated after the adjusted model.[31] We calculated the hypothetical total number of adverse birth outcomes that would have been observed had there been no women hospitalised for mental health disorders in the population (i.e., a zero counterfactual) by dividing the observed number of adverse birth outcomes by 1 minus the prevented fraction. The total number of adverse birth outcomes averted was then calculated by subtracting observed from hypothetical totals. A 95% CI range for the estimate of adverse birth outcomes averted was calculated with the lower and upper 95% CIs of the prevented fraction. We evaluated the robustness of the IRR to potential unmeasured confounding by

calculating an E-value.[32] We used Stata 17 for analysis and presented the results using figures and tables. The presentation of the findings from this study followed the Strengthening the Reporting of Observational Studies in Epidemiology (STROBE) guideline.[33]

Ethical clearance and role of funding source

The study was approved by the Human Research Ethics Committee of the Northern Territory Department of Health and the Menzies School of Health Research (HREC-2016-2708) and was supported by the First Nations Advisory Group for the Child and Youth Development Research Partnership which includes independent Aboriginal community members. The funder of the study had no role in study design, data collection, analysis, interpretation, or writing of this report. The research team had full access to all the data in the study and final responsibility for the decision to submit for publication.

Results

Of 72,518 births between the years 1999 and 2017, 2093 births were excluded because of a missing or an interstate residency record, or lack of key data such as the mothers' age, or Aboriginal status. 17,084 births were missing records on birth length. Our study cohort finally included a) 70,425 births for exploring PTB, LBW, and SB; and b) 53,341 births for exploring infant birth length (Fig. 1). Women whose record was not completed for the length of their newborn were more likely to be older, primigravida, and not hospitalised for mental disorders. The prevalence of maternal hospitalisation within 5 years of pregnancy for mental illness, substance misuse, and for both was 0.9%, 0.4%, and 0.2% among non-Aboriginal women; and 2.2%, 5.6%, and 1.2% among Aboriginal women, respectively. The prevalence of maternal hospitalisation during pregnancy for mental illness, substance misuse, and for both was 0.4%, 0.1%, and 0.03% among non-Aboriginal women and 0.7%, 1.9%, 0.2% among Aboriginal women, respectively (Figs. 1 and 2, Table 3 in Supplementary Information). No risk of misclassification by the time of exposure assessment was detected in both Aboriginal and non-Aboriginal populations for all categories of MHrH (Tables 4 and 5 in Supplementary Information).

3386 (7.6%; 95% CI: 7.3%, 7.8%) non-Aboriginal and 3990 (15.5%; 95% CI: 15.1%, 16.0%) Aboriginal births were preterm and 291 (0.65%; 95% CI: 0.58%, 0.73%) non-Aboriginal and 339 (1.3%; 95% CI: 1.2%, 1.5%) Aboriginal births were SBs. 2819 (6.3%; 95% CI: 6.1%, 6.5%) non-Aboriginal and 3747 (14.6%; 95% CI: 14.2%, 15.0%) Aboriginal births were LBW. 4590 (15.1%; 95% CI: 14.7%, 15.5%) non-Aboriginal and 5333 (23.3%; 95% CI: 22.7%, 23.8%) Aboriginal births had SBL (Figs. 3 and 4 in Supplementary Information). A LCA model with two classes, a class of high and low adverse birth outcomes, best fits the data compared to the one and the three-class model with the lowest AIC and BIC (Table 6 in Supplementary Information).

A class of high adverse birth outcomes (class 2), with a membership probability of 10.5%, contains a class of births with an estimated probability of 75.8% (95% CI: 74.6%, 76.9%) PTB, 84.1% (95% CI: 82.9%, 85.3%) LBW, 7.1% (95% CI: 6.5%, 7.7%) SBs, and 93.9% (95% CI: 93.0%, 94.7%) SBL. Births to Aboriginal women were around three times (aOR = 2.51; 95% CI: 2.38, 2.64) more likely to be in a class of high adverse birth outcomes. Births to women who were hospitalised for mental illness, substance misuse, or both were 28%

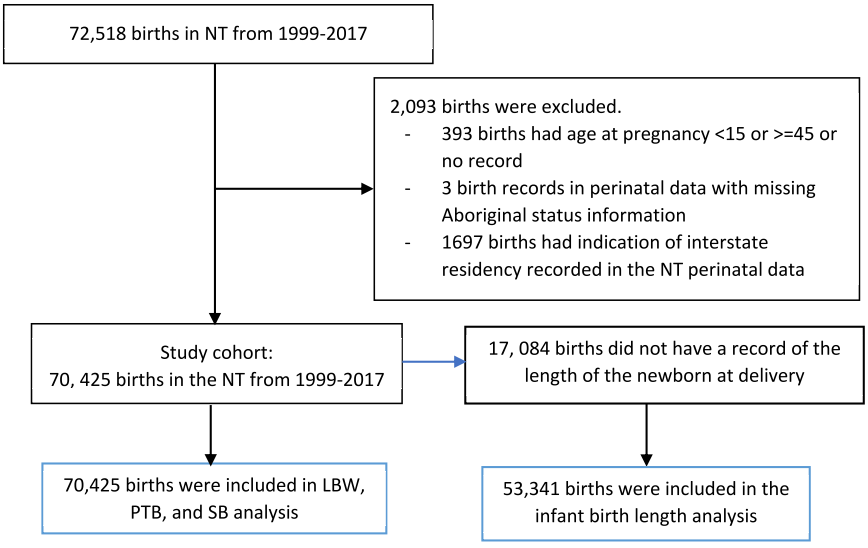

Fig. 1: Cohort selection for the study of adverse birth outcomes in the NT, Australia.

(aOR = 1.28; 95% CI: 1.05, 1.55), 76% (aOR = 1.76; 95% CI: 1.55, 2.01), and 97% (aOR = 1.97; 95% CI: 1.53, 2.53) more likely to be in a class of high adverse birth outcomes (Table 7 and Fig. 5 in Supplementary Information).

The incidence of PTB with maternal age followed a U-shaped curve with the lowest incidence observed in births to Aboriginal women in age 20–24 years and non-Aboriginal women in age 30–34 years old. The incidence of PTB was higher in Aboriginal (20.0%) and non-Aboriginal (15.8%) women hospitalised for substance misuse 5 years prior to pregnancy. The incidence of SB was slightly high in non-Aboriginal women in the youngest (0.7%) and in the oldest age group (0.9%) (Table 8 in Supplementary Information). After adjusting for all confounders, the risk of PTB was 20% (Adjusted Incidence Rate Ratio (aIRR) = 1.20; 95% CI: 1.05, 1.35) and 19% (aIRR = 1.19; 95% CI: 1.06, 1.34) higher in Aboriginal women with mental illness and substance misuse-related hospitalisation 5 years prior to pregnancy, respectively (Table 1). In Aboriginal women, alcohol use during pregnancy, ANC, and IUGR mediated the link between substance misuse-related hospitalisation 5 years prior to pregnancy and PTB by a total mediation effect of 9% (OR = 1.09; 95% CI: 1.05, 1.14) (Table 9 in Supplementary Information). The PAF for substance misuse-related hospitalisation 5 years prior to pregnancy was 16.1% (95% CI: 5.1%, 25.7%). The Population Preventive Fraction (PPF) of making at least eight ANC visits was 31.7% (95% CI: 29.8%, 34.3%) which saved about 1852 (95% CI: 1,694, 2083) extra PTBs in Aboriginal births (Table 10 in Supplementary Information).

The risk of PTB was 62% (aIRR = 1.62; 95% CI: 1.16, 2.26) higher in non-Aboriginal women hospitalised for substance misuse five years prior to pregnancy (Table 1). ANC and IUGR in non-Aboriginal women fully mediated the association between mental illness-related hospitalisation and PTB by a mediation effect of 10% (OR = 1.10; 95% CI: 1.02, 1.19), concurrent hospitalisation for mental illness and substance misuse and PTB by a mediation effect of 22% (OR = 1.22; 95% CI: 1.08, 1.38), and partially mediated the association between substance misuse-related hospitalisation and PTB by a mediation effect of 22% (OR = 1.22; 95% CI: 1.10, 1.35) (Table 10 in Supplementary Information). The PAF for PTB was 38.3% (95% CI: 13.8%, 55.7%) for non-Aboriginal women hospitalised for substance misuse 5 years prior to pregnancy. The PPF of at least eight ANC visits was 54.3% (95% CI: 52.0%, 56.7%) which saved about 4023 (95% CI: 3,668, 4434) extra PTBs in non-Aboriginal births (Table 12 in Supplementary Information).

No association was found between MHrH 5 years prior to and during pregnancy with the risk of SB in Aboriginal births. However, the risk of stillbirth was around four times (aIRR = 3.75; 95% CI: 1.29, 10.95) and eight times (aIRR = 7.89; 95% CI: 1.17, 53.37) higher in non-Aboriginal births with concurrent hospitalisation for mental illness and substance misuse 5 years prior to and during pregnancy, respectively (Table 1). ANC and alcohol consumption during pregnancy fully mediated the association between substance misuse-related hospitalisation 5 years prior to pregnancy and SB in Aboriginal pregnancies with a total mediation effect of 4% (OR = 1.04; 95% CI: 1.01, 1.08) (Table 9 in

Exposure	Preterm birth				Stillbirth			
	Aboriginal		Non-Aboriginal		Aboriginal		Non-Aboriginal	
	cIRR	aIRR	cIRR	aIRR	cIRR	aIRR	cIRR	aIRR
Reason for hospitalisation in the five years prior to pregnancy								
No (ref)								
Mental illness[a]	1.25 (1.05, 1.49)	1.20 (1.01, 1.41)[c]	1.38 (1.04, 1.83)	1.25 (0.94, 1.66)	1.12 (0.56, 2.25)	1.12 (0.56, 2.24)	1.84 (0.76, 4.43)	1.78 (0.75, 4.20)
Substance misuse	1.32 (1.19, 1.47)	1.19 (1.05, 1.35)[c]	2.12 (1.51, 2.96)	1.62 (1.16, 2.26)[c]	1.76 (1.22, 2.52)	1.16 (0.75, 1.79)	0.85 (0.12, 6.05)	0.64 (0.09, 4.33)
Both[b]	1.20 (0.94, 1.53)	1.04 (0.81, 1.33)	1.85 (1.16, 2.97)	1.51 (0.90, 2.54)	0.79 (0.26, 2.46)	0.61 (0.19, 1.93)	4.34 (1.41, 13.32)	3.75 (1.29, 10.95)[c]
Reason for hospitalisation during pregnancy								
No (ref)								
Mental illness[a]	0.95 (0.67, 1.36)	0.93 (0.66, 1.30)	1.89 (1.32, 2.70)	1.38 (0.98, 1.95)	0.87 (0.22, 3.46)	0.90 (0.23, 3.51)	0.00	0.00
Substance misuse	1.39 (1.17, 1.65)	1.15 (0.96, 1.37)	1.53 (0.72, 3.25)	1.02 (0.48, 2.15)	1.87 (1.06, 3.30)	1.07 (0.57, 2.00)	2.96 (0.42, 20.71)	2.06 (0.96, 4.41)
Both[b]	1.06 (0.54, 2.08)	0.90 (0.46, 1.76)	2.21 (0.62, 7.85)	1.54 (0.45, 5.30)	0.00	0.00	12.83 (1.96, 84.15)	7.89 (1.17, 53.37)[c]

[c]IRR is crude incidence rate ratio; [a]IRR is adjusted incidence rate ratio for maternal age, parity, pre-existing diabetes, pre-existing hypertension, gestational diabetes, pre-eclampsia or eclampsia; ANC visits, IUGR, smoking, alcohol consumption during pregnancy, administrative health districts, and history of adversity-related admissions; ref is reference category where the IRR is 1. [a]Encompasses (i) severe mental illness; (ii) common mental disorders; (iii) personality disorders; (v) all other adulthood-onset illness; and (vi) all other childhood-onset illness. [b]Defines women who experienced both mental illness and substance misuse. [c]Significant at p-value <0.05.

Table 1: **Association between maternal MHrH 5 years prior to and during pregnancy and risk of preterm birth and stillbirth among Aboriginal and non-Aboriginal birth cohorts from years 1999 to 2017 in NT, Australia.**

Supplementary Information). The highest PAF for SB in Aboriginal women was for women with complications of preexisting diabetes (56.0%; 95% CI: 25.5%, 73.9%). A PPF of making at least eight ANC visits was 41.0% (95% CI: 32.0%, 49.6%) which saved about 235 (95% CI: 159, 334) extra SBs in Aboriginal pregnancies (Table 10 in Supplementary Information). Similarly, attendance at eight or more ANC visits partially mediated the association between concurrent hospitalisation for mental illness and substance misuse 5 years prior to pregnancy and SB in non-Aboriginal pregnancies with a total mediation effect of 39% (OR = 1.39; 95% CI: 1.14, 1.69) (Table 10 in Supplementary Information). The PPF of making at least eight ANC visits was 71.4% (95% CI: 64.5%, 76.7%) which saved about 726 (95% CI: 529, 958) extra SBs in non-Aboriginal pregnancies (Table 12 in Supplementary Information).

The incidence of LBW with maternal age in both non-Aboriginal and Aboriginal women followed a U-shaped curve with the lowest incidence of LBW registered among births to Aboriginal women in the age category of 20–24 and non-Aboriginal women in the age category of 30–34. The incidence of SBL increased with maternal age in Aboriginal women and followed a U-shaped curve with non-Aboriginal women with the lowest SBL observed in women in the age category of 30–34 years (p = 0.000) (Table 13 in Supplementary Information). Substance misuse-related hospitalisation (aIRR = 1.23; 95% CI: 1.10, 1.39) and concurrent hospitalisation for substance misuse and mental illness (aIRR = 1.28; 95% CI: 1.04, 1.58) 5 years prior to pregnancy; and concurrent hospitalisation for substance misuse and mental illness (aIRR = 1.63; 95% CI: 1.01, 2.62) during pregnancy were associated with an increased risk of LBW in Aboriginal births (Table 2). In Aboriginal births, ANC, alcohol consumption and smoking during pregnancy, and IUGR mediated the link between substance misuse-related hospitalisation, concurrent hospitalisation with substance misuse and mental illness, and the risk of LBW with a total mediation effect of 14% (OR = 1.14; 95% CI: 1.07, 1.22) and 16% (OR = 1.16; 95% CI: 1.04, 1.30), respectively (Table 9 in Supplementary Information).

The PAF for LBW attributed to substance misuse-related hospitalisation and concurrent hospitalisation for substance misuse and mental illness 5 years prior to pregnancy in Aboriginal births was 18.6% (95% CI: 8.1%, 27.8%) and 21.9% (95% CI: 3.4%, 36.8%), respectively. The PAF for LBW attributed to concurrent hospitalisation for substance misuse and mental illness during pregnancy in Aboriginal births was 38.5% (95% CI: 0.8%, 61.8%). The PPF of making at least eight ANC visits was 32.8% (95% CI: 31.1%, 35.6%) which saved about 1829 (95% CI: 1691, 2071) extra LBW Aboriginal births (Table 10 in Supplementary Information).

The risk of LBW was around two times (aIRR = 1.96; 95% CI: 1.41, 2.73) higher in non-Aboriginal births to women exposed to substance misuse-related hospitalisation 5 years prior to pregnancy (Table 2). ANC partially mediated the path between substance misuse-related hospitalisation 5 years prior to pregnancy and LBW with a mediation effect of 22% (OR = 1.22; 95% CI: 1.13, 1.31) (Table 11 in Supplementary Information). The PAF of LBW in non-Aboriginal births that attributed to substance misuse-related hospitalisation in the 5 years prior to pregnancy was 48.9% (95% CI: 28.9%, 63.3%). The PPF of making at least eight ANC visits was 51.5% (95% CI: 48.1%, 53.8%) which saved about 2993 (95% CI: 2612, 3691) extra LBW non-Aboriginal babies (Table 12 in Supplementary Information).

Exposure	LBW(≤2500 g)				Short birth length (≤47 cm)			
	Aboriginal		Non-Aboriginal		Aboriginal		Non-Aboriginal	
	cIRR	aIRR	cIRR	aIRR	cIRR	aIRR	cIRR	aIRR
Reason for hospitalisation five years prior to pregnancy								
No (ref)								
Mental illness[a]	1.07 (0.87, 1.30)	1.03 (0.84, 1.25)	1.29 (0.93, 1.78)	1.05 (0.76, 1.45)	1.25 (1.08, 1.44)	1.20 (1.04, 1.38)[c]	1.46 (1.19, 1.79)	1.28 (1.06, 1.56)[c]
Substance misuse	1.45 (1.30, 1.61)	1.23 (1.10, 1.39)[c]	2.63 (1.89, 3.66)	1.96 (1.41, 2.73)[c]	1.40 (1.28, 1.52)	1.28 (1.16, 1.41)[c]	1.85 (1.43, 2.41)	1.45 (1.13, 1.86)[c]
Both[b]	1.62 (1.31, 2.00)	1.28 (1.04, 1.58)[c]	2.08 (1.28, 3.40)	1.21 (0.76, 1.95)	1.48 (1.25, 1.75)	1.20 (1.01, 1.43)[c]	2.82 (2.22, 3.59)	1.88 (1.44, 2.45)[c]
Reason for hospitalisation during pregnancy								
No (ref)								
Mental illness[a]	1.14 (0.82, 1.59)	1.23 (0.90, 1.69)	1.92 (1.29, 2.84)	1.06 (0.74, 1.53)	1.20 (0.93, 1.55)	1.23 (0.97, 1.57)	2.08 (1.65, 2.62)	1.47 (1.17, 1.84)[c]
Substance misuse	1.68 (1.43, 1.97)	1.15 (0.98, 1.35)	1.53 (0.67, 3.53)	0.76 (0.30, 1.92)	1.62 (1.43, 1.83)	1.23 (1.08, 1.40)[c]	1.74 (1.07, 2.84)	1.06 (0.65, 1.74)
Both[b]	1.94 (1.20, 3.14)	1.63 (1.01, 2.62)[c]	2.66 (0.75, 9.43)	1.57 (0.45, 5.51)	1.88 (1.30, 2.73)	1.52 (1.05, 2.19)[c]	3.34 (1.90, 5.89)	1.97 (1.14, 3.41)[c]

[c]IRR is crude incidence rate ratio; [a]IRR is adjusted incidence rate ratio for maternal age, parity, pre-existing diabetes, pre-existing hypertension, gestational diabetes, pre-eclampsia or eclampsia; ANC visits, IUGR, smoking, alcohol consumption during pregnancy, administrative health districts, and history of adversity-related admissions; ref is reference category where the IRR is 1. [a]Encompasses (i) severe mental illness; (ii) common mental disorders; (iii) personality disorders; (v) all other adulthood-onset illness; and (vi) all other childhood-onset illness. [b]Defines women who experienced both mental illness and substance misuse. [c]Significant at p-value <0.05.

Table 2: **Association between maternal MHrH 5 years prior to and during pregnancy, and risk of low birth weight and short birth length among Aboriginal and non-Aboriginal birth cohorts from years 1999 to 2017 in NT, Australia.**

After adjusting for potential confounders, all categories of maternal MHrH in the 5 years prior to pregnancy were associated with risk of SBL in both populations. Maternal hospitalisation for mental illness, substance misuse, and for both disorders in the 5 years prior to pregnancy were associated with 20% (aIRR = 1.20; 95% CI: 1.04, 1.38), 28% (aIRR = 1.28; 95% CI: 1.17, 1.41), and 20% (aIRR = 1.20; 95% CI: 1.01, 1.43) increased risk of SBL in Aboriginal births (Table 2). Aboriginal births to women hospitalised for substance misuse and concurrently hospitalised for substance misuse and mental illness during pregnancy had a 23% (aIRR = 1.23; 95% CI: 1.08, 1.40) and 52% (aIRR = 1.52; 95% CI: 1.05, 2.19) high risk of SBL (Table 2). Alcohol use during pregnancy, ANC, and IUGR mediated the path between substance misuse-related hospitalisation 5 years prior to pregnancy and SBL in Aboriginal births with a mediation effect of 9% (OR = 1.09; 95% CI: 1.05, 1.13).

Alcohol use and smoking during pregnancy, ANC, and IUGR mediated the path between concurrent mental-illness and substance misuse-related hospitalisation in the 5 years prior to pregnancy and SBL in Aboriginal births with a mediation effect of 10% (OR = 1.10; 95% CI: 1.02, 1.19) (Table 9 in Supplementary Information). The PAF of SBL attributed to mental illness-related hospitalisation, substance misuse-related hospitalisation, and concomitant hospitalisation for both disorders in the 5 years prior to pregnancy were 16.5% (95% CI: 3.8%, 27.6%), 21.9% (95% CI: 14.1%, 29.1%), and 16.8% (95% CI: 1.0%, 30.1%), respectively. The PPF of making at least eight ANC visits was 20.8% (95% CI: 18.8%, 23.0%) which saved about 1400 (95% CI: 1235, 1593) extra SBL Aboriginal babies (Table 10 in Supplementary Information). Maternal hospitalisation for mental illness, substance misuse, and for both disorders in the 5 years prior to pregnancy increased the risk of SBL in non-Aboriginal births by 28% (aIRR = 1.28; 95% CI: 1.06, 1.56), 45% (aIRR = 1.45; 95% CI: 1.13, 1.86), and 88% (aIRR = 1.88; 95% CI: 1.44, 2.45), respectively.

The risk of SBL was 47% (aIRR = 1.47; 95% CI: 1.17, 1.84) and 97% (aIRR = 1.97; 95% CI: 1.14, 3.41) higher among non-Aboriginal births to mothers hospitalised for mental illness and concomitantly hospitalised for both disorders during pregnancy, respectively (Table 2). IUGR mediated the path between mental illness-related hospitalisation and risk of SBL in non-Aboriginal births by a mediation effect of 8% (OR = 1.08; 95% CI: 1.01, 1.14). Eight or more ANC visits mediated the path between substance misuse-related hospitalisation and concurrent hospitalisation for both disorders in the 5 years prior to pregnancy and risk of SBL in non-Aboriginal births by a total mediation effect of 9% (OR = 1.09; 95% CI: 1.02, 1.16) and 11% (OR = 1.11; 95% CI: 1.03, 1.19), respectively (Table 11 in Supplementary Information). The PAF of SBL in non-Aboriginal births that attributed to mental illness-related hospitalisation, substance misuse-related hospitalisation, and to concomitant hospitalisation for both disorders in the 5 years prior to pregnancy were 22.1% (95% CI: 5.3%, 35.9%), 31.1% (95% CI: 11.8%, 46.2%), and 46.7% (95% CI: 30.3%, 59.2%), respectively. The PPF of attending at least eight ANC visits was 32.2% (95% CI: 29.6%, 34.9%) which saved about 2180 (95% CI: 1930, 2461) extra SBL non-Aboriginal births (Table 12 in Supplementary Information).

Discussion

This study is the first to evaluate the association between maternal MHrH 5 years prior to or during pregnancy and adverse birth outcomes using administratively collected and linked data in Northern Territory, Australia. Births to Aboriginal women who had a MHrH in the 5 years prior to pregnancy were around three times more likely to be in a latent class of high adverse birth outcomes. Substance misuse-related hospitalisation in the 5 years prior to pregnancy increased the risk of preterm, LBW, and SBL in both populations. Mental illness-related hospitalisation 5 years prior to pregnancy increased the risk of PTB in Aboriginal births and SBL in both Aboriginal and non-Aboriginal births. Concomitant hospitalisation for mental illness and substance misuse in the 5 years prior to pregnancy and during pregnancy increased the risk of SB in non-Aboriginal births.

Our study replicates previous findings that maternal MHrH before or during pregnancy increases the risk of PTB and LBW in both non-Aboriginal and Aboriginal women.[5,6,13,34] We propose four potential pathways to explain this link: i) MHrH effects are mediated by obstetric complications leading to adverse birth outcomes; ii) Women with psychiatric diagnoses are more likely to engage in behaviours such as smoking and alcohol consumption during pregnancy, which can lead to poor fetal growth and subsequent adverse birth outcomes; iii) Biological and hormonal pathways involving psychiatric symptoms lead to elevated cortisol production or plasminogen activator inhibitor 1 (PAI-1), which can adversely alter the intrauterine environment and contribute to adverse birth outcomes[35]; and iv) mental health disorders affects maternal health service uptake including ANC—our study demonstrated that ANC service attendance mediated most of the paths from pre-pregnancy maternal MHrH to adverse birth outcomes — and attending at least eight ANC service demonstrated to prevent a significant number of adverse birth outcomes.[36,37] Prior evidence regarding the association between maternal MHrH and SB is inconsistent.[13,34] Our study finding substantiates those findings that reported association between maternal MHrH and SB. Infant birth length is the strongest predictor of linear growth status in early childhood[38] where the link between maternal mental health condition and birth length has never been explored.

The highest incidence of adverse birth outcomes was attributed to lack of eight or more ANC visits and IUGR while these two factors also played an important role in explaining the paths between maternal MHrH and adverse birth outcomes. Cortisol dysregulation linked to maternal mental health conditions around pregnancy may contribute to fetal growth restriction, subsequently leading to adverse birth outcomes.[39,40] The importance of ANC service in preventing adverse perinatal outcomes through early identification and treatment of risks such as IUGR is highly replicable.[41] Screening IUGR help for identification of potential risks such as fetal demise or perinatal complications, which may enable timely intervention through proper monitoring and optimized delivery. Identification of IUGR is often not straightforward as fetal growth cannot be assessed through a single biometric evaluation of the fetal size, and growth potential is hypothetical.[42–44] However, the combined use of symphysis-fundal height (SFH), ultrasound, and growth charts have been reported to improve screening precision for fetal growth restriction.[45,46] Randomised trials investigating interventions to mitigate IUGR are still ongoing,[47] however there is existing evidence supporting the benefits of proper nutrition and stress management during pregnancy. For example, two population-based cohort studies conducted in Spain revealed that increased consumption of fish, legumes, and dairy products reduced risk of fetal growth restriction.[48] Further exploration of the link between nutrition intervention and stress management in pregnancy, and other primary risk factors of IUGR in Australian context would be essential to develop an adaptable intervention.

Our study demonstrates a significant population-level impact of maternal MHrH occurring in the 5 years prior to pregnancy, which is consistent with previous research.[5,7,8] The highest incidence of SB in non-Aboriginal births was attributed to concomitant hospitalisation for mental illness and substance misuse during pregnancy. A significant incidence of adverse birth outcomes in Aboriginal (PAF ~ 25%) and non-Aboriginal (PAF ~ 40%) births was attributed to MHrH in the 5 years prior to and during pregnancy and could be averted if we could prevent MHrH in childbearing age women. Aboriginal pregnancies showed a two-fold increased likelihood of maternal MHrH and adverse birth outcomes compared to non-Aboriginal pregnancies.[8] Structural health inequalities are likely to be contributing to the disproportionate adverse outcomes.[15] A known barrier preventing Aboriginal women from disclosing past or current mental health problems and engagement with treatment is stigma and a fear that their baby will be taken away.[49]

Implications

Our study has significant public health, clinical, and research implications particularly for Aboriginal populations in Australia and beyond. The public health implications of our study underscore the need for establishing or enhancing community mental health prevention services. Recent policy priorities in global mental health have focused on closing the treatment gap and the current global mental health action plan also prioritises the promotion and prevention of mental health.[50] The Sustainable Development Goals (SDGs) commit countries to reduce premature mortality from non-communicable disease through promoting mental health and wellbeing.[51] However, the recent Lancet Commission on Global Mental Health and Sustainable Development emphasised a lack of progress in most nations; and challenging every nation to address service gaps.[52] Mental health services could be integrated into various settings, including schools, workplaces, detention centres, and other points of public contact. Digital resources, such as web-based content, social media, and telemedicine can also play a crucial role in reaching widely and fast. Such digital resources can provide mental health information, self-screening tools, and individual or group-based psychotherapy, thereby enhancing access to maternal mental health support and reducing social stigmatisation.[53,54] The efficacy of targeted mental health interventions compared to population-level approaches remain uncertain; however, it is advisable to continually assess progress for a more informed understanding.[55]

From a clinical perspective, our study supports recent campaigns on promoting preconception health[56,57] as the evidence regarding the use or avoidance of medical interventions for treating mental disorders during pregnancy has been inconclusive.[34,58–61] Interventions focusing on prevention rather than treatment of mental health disorders around pregnancy are crucial. The effect of a Birthing on Country service in improving Aboriginal women's ANC attendance and reducing preterm birth has been demonstrated and needs to be strengthened to narrow the gap in outcome between Aboriginal and non-Aboriginal populations.[62] Preconception health emphasises the importance of inclusive preconception care models that seamlessly integrate mental health and maternal health services. Service integration can be achieved through risk-based or universal approaches, catering to diverse preconception care needs. Risk-based approaches could involve prioritising women at higher risk of mental health disorders during perinatal care service visits using culturally safe psychosocial risk assessment tools. Adopting a universal approach would involve developing comprehensive preconception care guidelines and providing both paper-based and digital tools for self-assessment of preconception health risks. Additionally, guidance on seeking appropriate advice based on assessment results should be included.[63] The Canadian PreCHART is an example of an extensively developed and tested digital tool for assessing preconception health risks, offering

advantages to both providers and clients engaged in pregnancy planning.[64] Furthermore, pharmacists can play a crucial role in enhancing preconception care for women using medications for mental health-related disorders by identifying risks, providing counseling, and facilitating linkage to appropriate services.[65,66] Women with moderate to severe mental health conditions during pregnancy should receive management within a clinical setting, considering individualised risk-benefit analyses and the potential impact of medication on perinatal outcomes.[67]

As a research implication, our study highlights fetal developmental complications specifically IUGR as an important pathway to all adverse birth outcomes except stillbirth in both non-Aboriginal and Aboriginal populations. As such, further exploration is needed to understand the nature and pattern of these complications, enabling targeted interventions to effectively mitigate the risk of adverse birth outcomes attributed to IUGR.

This study acknowledges limitations related to data quality and access to potential covariates such as educational, household income, marital status, partner support, maternal nutritional status etc. that would confound the link between exposure and outcomes, which may introduce residual confounding bias. The use of hospital records for maternal MHrH may underestimate the true prevalence within the general population. Efforts were made to address this by including multiple diagnostic codes. Despite these limitations, the study considered various maternal and psychosocial factors to minimise confounding. The inclusion of a perinatal cohort from the Northern Territory over an 18-year period enhances the generalisability of the findings. Our study is a significant contribution given the limited and inconsistent prior research on this topic in other Australian states. It highlights the need for further investigations and sets the stage for future studies to optimise perinatal mental health to improve both maternal and child outcomes.

Conclusion

Maternal MHrH prior to and during pregnancy and the incidence of adverse birth outcomes were disproportionately higher among Aboriginal population. Maternal MHrH 5 years prior to pregnancy partially to fully accounted for an increased risk of all adverse birth outcomes in both populations. Alcohol use during pregnancy, eight or more ANC attendance, and IUGR played a significant role in explaining the link between maternal MHrH 5 years prior to pregnancy and the risk of adverse birth outcomes. A significant incidence of adverse birth outcomes in both non-Aboriginal and Aboriginal populations were attributed to maternal MHrH 5 years prior to and during pregnancy, which could be averted by implementing both community and clinical-based preconception care. Eight or more ANC visits prevented, on average, around 30% of Aboriginal babies and over 60% non-Aboriginal babies from LBW, PTB, and SB, highlighting both the need to improve access to ANC and outcomes for Aboriginal babies.

Contributors

AFD conceived the idea, designed, analysed the data, and prepared a draft manuscript. VH and SG actively participated in design, data preparation, analysis, and finally made a critical review of the manuscript. All authors critically reviewed the manuscript for content, methodological validity, sound interpretation of the findings, and agreed for the decision to submit the manuscript for publication.

Data sharing statement

The study datasets contain potentially identifying or sensitive patient information and are held on a secure cloud-based server with restricted access. The data can be available upon request and approval of ethics committee and data custodians.

Declaration of interests

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Appendix A. Supplementary data

Supplementary data related to this article can be found at https://doi.org/10.1016/j.lanwpc.2024.101063.

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