Evaluating the relationship between hepatitis B viral activity and gestational diabetes mellitus: a prospective cohort study

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1. Background

- Chronic hepatitis B virus infection (CHB) during pregnancy has been associated with the development of gestational diabetes mellitus (GDM), particularly in women of South East Asian ethnicity, who have a higher prevalence of both conditions.
- The underlying mechanism is not well characterised, but may be due to the chronic inflammatory state associated with CHB

2. Objectives

To examine associations between hepatitis B viral activity and GDM in pregnant people with CHB

3. Methods

Study design

- Three maternity centres in Melbourne providing care cumulatively for nearly 30 000 pregnant women/year
- Conducted May 2021- April 2023

Variables collected

- Demographics and markers of viral activity (Table 1)
- Antivirals prescribed in accordance with recommended clinical guidelines

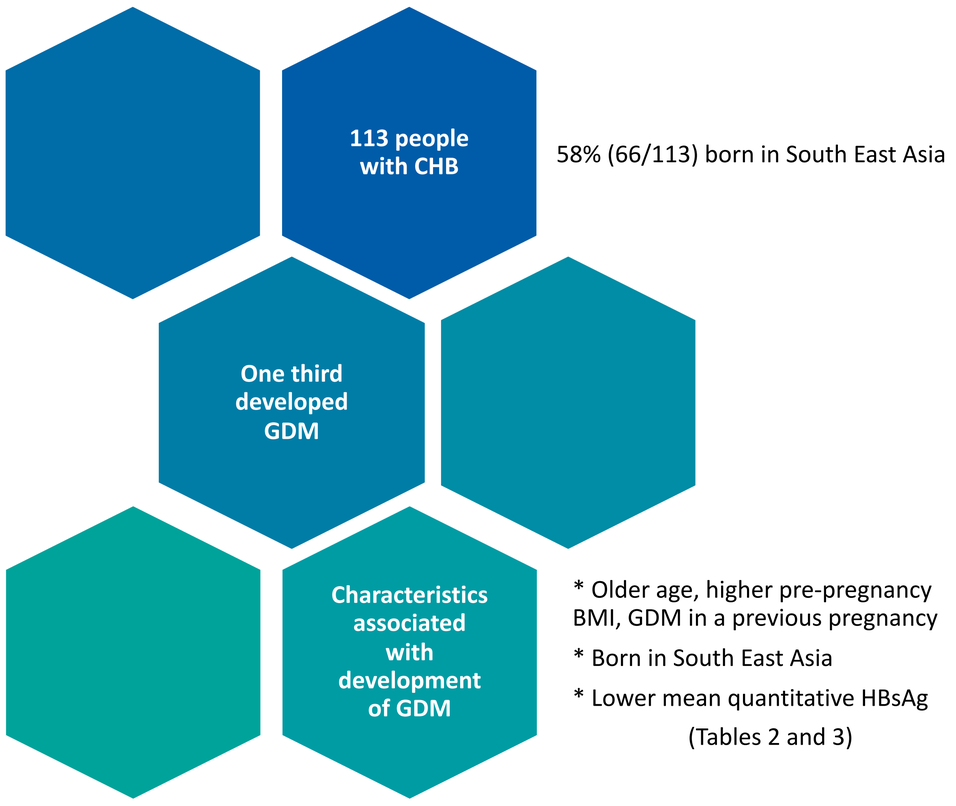
Table 1: Variables collected

Maternal demographics	Markers of Hepatitis B viral activity
Age	Liver function tests
BMI	Hepatitis B viral load
Smoking	Hepatitis B e-antigen
Parity	Quantitative hepatitis B surface antigen (quantHBsAg)
Region of birth	
Comorbidities	
Previous GDM	
Family history of diabetes	

Statistical Analysis

Multivariable logistic regression adjusting for following known confounders (maternal age, body mass index (BMI), country of birth, past history of GDM, method of GDM diagnosis)

4. Results



58% (66/113) born in South East Asia

* Older age, higher pre-pregnancy BMI, GDM in a previous pregnancy
* Born in South East Asia
* Lower mean quantitative HBsAg

(Tables 2 and 3)

Table 2: Demographics

Maternal characteristic	Total cohort (n=113)	With GDM[a] (n=38)	Without GDM[a] (n=74)	p-value
Mean age (SD)	32 (5)	34 (5)	31.5 (45)	0.004
Mean BMI (SD)	25 (5)	27 (6)	25 (5)	0.05
Smoking (n,%)	2 (2%)	2 (5%)	0	0.115
Region of birth (n,%)				0.07
Australia & Oceania	6 (5%)	2 (5%)	4 (5%)	
Europe	7 (6%)	1 (3%)	6 (8%)	
Africa & Middle East	15 (13%)	3 (8%)	12 (16%)	
South-East Asia	66 (58%)	29 (76%)	36 (49%)	
Rest of Asia	19 (17%)	3 (8%)	16 (22%)	
Any comorbidity (n,%)	9 (8.0%)	4 (10.5%)	5 (6.8%)	0.485
Previous GDM (n,%)	20 (18%)	13 (34%)	7 (9.5%)	0.001
Family history of diabetes (n,%)	29 (26%)	11 (29%)	18 (24%)	0.738
Antiviral use (n, %)	23 (20%)	7 (18%)	16 (22%)	0.7

[a] One patient had no testing for GDM and was excluded from analysis

Table 3: Markers of viral activity

	With GDM[a] (n=38)	Without GDM[a] (n=74)	p-value
Viral load (n,%)			0.4
Low (<2000 IU/ml)	29 (76%)	52 (70%)	
High (>2000IU/ml)	8 (21%)	22 (30%)	
Unknown	1 (3%)	0	
Mean ALT (SD)	21 (10)	24 (21)	0.5
Mean ALP (SD)	63 (33)	65 (29.5)	0.6
Mean GGT (SD)	18 (11)	18 (12)	0.8
Mean bilirubin (SD)	6.5 (2)	8 (4)	0.07
Mean albumin (SD)	34 (4)	33 (4)	0.3
Mean ferritin (SD)	78 (78)	73 (84)	0.8
HBeAg status n=96 (n,%)			0.9
Positive	7 (18)	14 (19)	
Negative	26 (68)	49 (66)	
Unknown	5 (13)	11 (15)	
Quantitative sAg n=59 (n,%)			
Mean (SD)	1948 (2774)	4449 (6460)	0.04
High (>100 IU/ml)	13 (34%)	30 (40%)	0.2
Low (<100 IU/ml)	8 (21%)	8 (11%)	
Unknown	17 (45%)	36 (49%)	

[a] One patient had no testing for GDM and was excluded from analysis

Table 4: Multivariable logistic regression of markers of viral activity and association with GDM

	Adjusted Odds Ratio (95% CI)	p-value
High viral load (>2000 IU/ml)	0.8 (0.3–2.5)	0.4
HBeAg positive	1.8 (0.3–2.6)	0.75
Antiviral use	1.8 (0.3–2.5)	0.7
ALT_{10} (U/L)	0.8 (0.5–1.1)	0.2
$Ferritin_{10}$ (µg/L)	1.0 (0.95–1.1)	0.9
GGT_{10} (U/L)	0.9 (0.6–1.3)	0.5
ALP_{10} (U/L)	1.05 (0.8–1.25)	0.6
Bilirubin (µmol/L)	0.9 (0.7–1.0)	0.06
Quantitative HBsAg >100 IU/ml	0.6 (0.6–2.7)	0.5

Each marker of viral activity was assessed by logistic regression model with covariables of age, BMI, SE Asia country of birth, method of GDM diagnosis and past history of GDM. Where value is denoted with $subscript_{10}$ this indicates that statistical values relate to changes per 10 units. – Unable to be calculated accurately within model due to low cell values.

5. Conclusion

Participants with CHB were diagnosed with GDM at almost twice the rate of women undergoing antenatal care in Australia but similar to reported rates of GDM in women of South East Asian ethnicity.
Quantitative HBsAg may be a useful surrogate marker to predict GDM, to allow earlier diagnosis, education and monitoring but requires further studies in other settings to confirm our findings.

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