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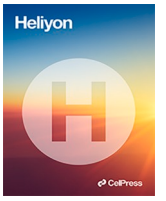

Research article

Association of antenatal anxiety disorders with antenatal comorbidities and adverse pregnancy outcomes among clinic attendees at a tertiary-care hospital in Sri Lanka

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ABSTRACT

Purpose: Evidence on the association between antenatal anxiety disorders (AADs) and adverse pregnancy outcomes with detection of AADs using the gold-standard is scarce despite being vital to make decisions on interventions. We aimed to determine this association in women attending tertiary-care antenatal clinics in Sri Lanka.

Material and methods: Presence/absence of AADs in a systematic random sample of 221 antenatal women attending routine antenatal clinics of a teaching hospital who participated in a questionnaire-validation study were confirmed by a psychiatrist. These women were followed up until the end of pregnancy. Information on antenatal comorbidities, adverse pregnancy outcomes was extracted from health records. The association between AADs with antenatal comorbidities and adverse pregnancy outcomes were reported using adjusted odds ratios (ORs) and 95%confidence intervals (CIs) generated from logistic regression models.

Results: Mean (±SD) age of the women was 30 (±5.8) years. AADs were diagnosed in 81 (37%) women. Compared to women without AADs, those who had AADs were more at risk of pregnancy-induced hypertension (OR 6.1; 95% CI 1.2–31.9), gestational diabetes mellitus (OR 12.6; 95% CI 1.5–107.2), preterm labour (OR 4.3; 95% CI 1.4–13.0), prolonged labour (OR 19.0; 95% CI 7.1–51.1), lower segment caesarean section (OR 4.7; 95% CI 2.5–8.7) and low birthweight (OR 11.2; 95% CI 4.8–26.3). All miscarriages, stillbirths and assisted labour occurred exclusively in those with AADs.

Conclusions: AADs are strongly associated with several adverse pregnancy outcomes. Causal pathways and effect of interventions for AADs must be explored in future research.

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1. Introduction

Pregnancy often causes some anxiety that is considered normal in antenatal women [1]. Anxiety disorders are also common during antenatal period partly due to increased susceptibility of women to early onset or relapse of such conditions during pregnancy [2]. Antenatal anxiety disorders (AADs) are often due to women worrying on parenting and/or maternal role, the wellbeing of the baby, hospital admission and healthcare-related experiences during childbirth and postpartum period [3]. There is limited evidence that these AADs may be associated with adverse foetal and maternal outcomes [4] including miscarriages, stillbirths, intrauterine growth restriction (IUGR), prolonged labour, lower segment caesarean section (LSCS), preterm labour and low birth weight (LBW) [3,5]. Consequences of AADs may additionally include long-term effects such as mental disorders, emotional problems, lack of concentration and hyperactivity in childhood [6].

However, most of the current evidence for the association between AADs and adverse pregnancy outcomes are based on studies that used screening-questionnaires rather than the gold-standard to diagnose AADs. The gold-standard of anxiety is the diagnosis by a psychiatrist after conducting a detailed interview [7] based on the International Classification of Diseases and Related Health Problems (ICD-10) which specifies the inclusion and exclusion criteria for the diagnosis but allows a degree of flexibility in diagnostic decision making in a clinical setting [8,9].

Furthermore, the association between AADs and adverse pregnancy outcomes remain mostly unknown in South Asian cultures, despite the fact that occurrence of AADs could be culture-specific [10] and some adverse pregnancy outcomes such as LBW due to AADs being reportedly higher in Asian women than in women in other regions [3]. Adverse pregnancy outcomes such as IUGR, preterm birth, low birth weight, newborn resuscitation at birth, and the need for neonatal intensive care units are Sri Lankan public health concerns. When considering the health indices on maternal and child health of Sri Lanka, Low birth weight, stillbirth rate, and neonatal mortality rates are 12.3%, 6.5%, and 7% per 1000 live births respectively. In addition, 31% of Sri Lankan women undergo caesarean-section and their antenatal and postnatal morbidities rates are 42% and 12% respectively [11]. We aimed to address these knowledge gaps by using the gold-standard to diagnose AADs in Sri Lankan antenatal women and determining its association with subsequent adverse pregnancy outcomes.

2. Material and methods

We previously conducted a validation study to determine the validity and reliability of Perinatal Anxiety Screening Scale among women attending antenatal clinics (ANCs) of Colombo South Teaching Hospital (CSTH) which is a tertiary care hospital in Colombo, the capital district of Sri Lanka. The CSTH is the second largest government hospital in this district [12] and provide care to antenatal women from many areas of Colombo District, especially from its southern suburbs. The methodology of this validation study and its findings were published elsewhere [13].

In brief, the women aged at least 18 years were recruited for this validation study regardless of their period of gestation from September 1, 2017 to November 30, 2017. Using the register of antenatal women as the sampling frame, systematic random sampling with a sampling interval of 5 was used to recruit these women. Those who had hearing or visual or speech problems, or could not give consent due to moderate to severe learning disabilities were excluded. A psychiatrist then determined the presence or absence of AAD based on International Classification of Diseases and Related Health Problems-10 (ICD-10) criteria [9]. The final sample consisted of 81 women with anxiety disorder and 140 women without anxiety disorder. The same antenatal women recruited in the validation study were followed up in this component of the study.

Upon completion of the diagnostic interview, participants responded to a questionnaire on socio-demographic and health-related information administered by a trained nurse. Their filed antenatal record numbers, telephone numbers, expected date of delivery, and respective field midwives' information were collected to enable subsequent tracing of their field health records from field midwives. These field midwives provide field-based routine antenatal care and collect relevant data. A continuous follow-up of these women until their delivery was precluded due to resource limitations but the PI contacted all women about a week prior to delivery and daily thereafter until delivery. The PI then visited the hospital and extracted relevant information from health records in the hospital [bedhead tickets and labour-room records] of the women in the original sample who delivered within the preceding week. These information included data on antenatal comorbidities including pregnancy-induced hypertension (PIH) and gestational diabetes mellitus (GDM) and information related to the pregnancy outcomes including gestational age at delivery, type of labour (spontaneous/assisted labour), mode of delivery (normal vaginal delivery [NVD],vacuum extraction, forceps delivery or lower-segment caesarean section [LSCS]), prolonged labour, stillbirths and birthweight. Information on miscarriages were taken from the records available with field midwives of the respective women's home area. The information extracted from hospital records were also verified by cross-checking with the records available with field midwives.

Prolonged labour was defined as (a) prolonged active phase of labour or (b) irregular or poor uterine contractions or (c) a labour with regular uterine contractions for more than 12 h or (d) a cervical dilation of 10 cm for more than 3 h [14]. Low birthweight (LBW) was defined as birthweight of $<$2500 g [15]. Preterm births (PTB) were defined as a birth before 37 weeks of gestation [15]. Definitions of other pregnancy outcomes are given in the online supplement [Table S1].

Informed written consent was obtained from all women. This study was conducted in accordance with the amended Declaration of Helsinki and was approved by the Ethics Review Committee of the Faculty of Medical Sciences, University of Sri Jayewardenepura, Sri Lanka (ERC ref. No: 25/27, May 2017).

2.1. Statistical analysis

Descriptive data are reported as numbers and percentages or means and standard deviations (SDs). The association between AADs and adverse pregnancy outcomes were examined using multivariate logistic regression method controlled for the known confounders and are presented as odd ratios (ORs) and 95% confidence intervals (CIs). Because the sample size was calculated for a different study, we calculated the statistical power this study had to detect some of the adverse pregnancy outcomes [16,17,18]. These were 34% for preterm labour, 37% for LBW, and 99% for LSCS.

3. Results

The basic characteristics of those with and without anxiety are shown in Table 1.

As we previously reported [13] 36.65% (n = 81) of women had AADs, and these AADs were mild in 58.0% (n = 47; Table 2). Phobias (39.5%) and generalized anxiety disorder (37.0%) were the commonest manifestations of AADs (Table 2; [13]).

3.1. Association of AADs with antenatal comorbidities and adverse pregnancy outcomes

Antenatal comorbidities and all adverse pregnancy outcomes that were assessed were significantly commoner in women with AADs (Fig. 1 and Table 3). Antenatal comorbidities associated with AADs were PIH (OR 6.1; 95% CI 1.2–31.9), GDM (OR 12.6; 95% CI 1.5–107.2). Maternal outcomes associated with AADs were preterm labour (OR 4.3; 95% CI 1.4–13.0), prolonged labour (OR 19.0; 95% CI 7.1–51.1) and LSCS (OR 4.7; 95% CI 2.5–8.7). AADs were also associated with low birthweight in the neonate (OR 11.2; 95% CI 4.8–26.3). All miscarriages, stillbirths and assisted labour occurred exclusively in those with AADs, and therefore, the ORs for those associations could not be meaningfully calculated.

4. Discussion

We investigated the association between AADs with antenatal comorbidities and pregnancy outcomes in a cohort of antenatal women who attended a tertiary-care hospital in Sri Lanka and found that 36.65% of them had AADs. We also found that AADs were significantly associated with several subsequent adverse pregnancy outcomes.

Detecting AADs using the gold standard for diagnosis is the main strength of our study. Most previous studies that investigated the

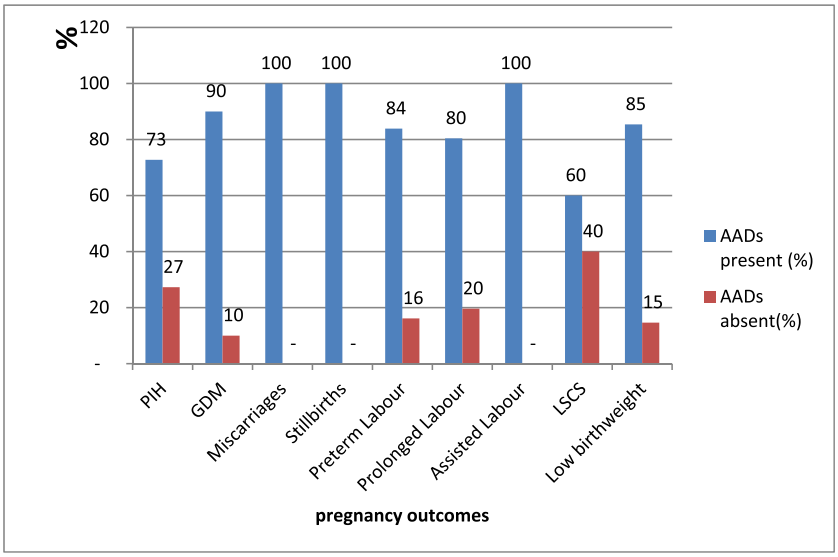
Table 1
Basic characteristics of the antenatal women (N = 221).

Variable	AADs absent (N = 140)		AADs present (N = 81)	
	n	%	n	%
Age (Years)[a]				
18–23	19	13.6	11	13.6
24–29	48	34.3	32	39.5
30–35	52	37.1	23	28.4
36–41	21	15.0	15	18.5
Level of Education				
No schooling	1	0.7	1	1.2
Completed Grade 11	113	80.7	62	76.5
Completed Grade 13	26	18.6	18	22.2
Average household monthly income Level (LKR)				
0–20000	78	55.7	40	49.3
20001–40000	28	20.0	14	17.2
40001–60000	0	0	0	0
60001–80000	9	6.4	9	11.1
80001–100000	3	2.1	7	8.6
100001 and above	22	15.7	11	13.6
Pregnancy and childbirth status				
First pregnancy [No living children]	60	42.9	37	45.7
Has one living child	51	36.4	43	53.0
Has two living children	22	15.7	1	1.2
Has three living children	6	4.3	0	0
Has four living children	0	0	0	0
Has five living children	1	0.7	0	0
Trimester in pregnancy at the time of recruitment				
Trimester1	18	12.9	14	17.3
Trimester 2	50	35.7	31	38.3
Trimester 3	72	51.4	36	44.4

AADs –Antenatal anxiety disorders.
LKR - Sri Lankan rupees.
[a] The mean (±SD) age of women with and without AADs were 29 (±5.7) and 29 (±5.9) years, respectively.

Table 2
Severity and domains of anxiety (N = 81).

Variable	n	%
Severity of anxiety		
Mild	47	58.0
Moderate	31	38.3
Severe	03	3.7
Domains of anxietyrowhead		
Phobias (blood and injection)	32	39.5
Generalized anxiety disorder	30	37.0
Social phobia	06	7.4
Panic disorder	06	7.4
Specific fear (Child birth)	04	4.9
OCD	02	2.5
PTSD	01	1.2



AADS- antenatal anxiety disorders

Fig. 1. Antenatal comorbidities and adverse pregnancy outcomes of women with antenatal anxiety disorders (81 antenatal women with antenatal anxiety disorders and 140 antenatal women without antenatal anxiety disorders).

association of anxiety with obstetrics outcomes had used screening questionnaires to detect AADs [19,20] instead of the gold standard. Only a few previous studies [20,21] including one in Asia [20] had used the gold standard for diagnoses.

We found that AADs were associated with antenatal comorbidities including PIH and GDM. An association between AADs and PIH was reported also in previous studies [20,22] conducted in United States of America and India respectively. However, to the best of our knowledge, our study is the first to report that AADs is associated with incident of GDM. Some previous studies reported that GDM caused severe level of anxieties during pregnancy [23,24] while Wilson et al. [25], reported that anxiety is not associated with GDM. These mixed findings suggest that the association between GDM and AADs could be bidirectional, The association of AADs with these medical comorbidities is likely to be due to AADs-induced high maternal cortisol level [26] which then leads to adverse pregnancy outcomes including PIH [27] and GDM [3,28]. The AADs increases maternal cortisol level further by impairing function and gene expression of placental 11β-hydroxysteroid dehydrogenase type 2 (11βHSD2), the enzyme which converts cortisol to the inactive cortisone. The high AADs reduces placental 11βHSD2 level leading to several adverse pregnancy outcomes [29].

The current evidence on the association of AADs with some labour-related outcomes are equivocal. The findings of our study will thus supplement this evidence. Although a positive association between AADs and prolonged labour has previously been shown [30,31,32], the previous evidence for the association between AADs and LSCS are equivocal [32,33,34,35]. It is possible that prolonged labour due to AADs [30], may then result in obstetric interventions such as LSCS or vacuum or forceps deliveries [36]. The high proportion of blood and injection phobia seen in our study may also have a role in this association. Women with specific anxieties such as blood and injection phobia more often fear childbirth [37] and more frequently experience incidence of prolonged labour and/or LSCS [38].

Associations of AADs with PTB and LBW were reported in most of the previous studies [3,20,34,39], while two studies reported no

Table 3
Association of antenatal anxiety disorders [AADs] with antenatal comorbidities and adverse pregnancy outcomes (N = 221).

Assessment Variable	AADs present (N = 81)		AADs negative (n = 140)		Unadjusted		Adjusted	
	n	%	n	%	Odds Ratio (95% CI)	p value	Odds Ratio (95% CI)	p value
Antenatal comorbidities								
PIH	8	72.7	3	27.2	4.6 (1.2–17.8)	0.02	6.1 (1.2–31.9)	0.032[a]
GDM	9	90	1	10	16.0 (2.0–128.0)	0.001	12.6 (1.5–107.2)	0.02[b]
Labour Outcomes								
Miscarriages	5	100	0	0	1.1 (1.0–1.1)	0.003	–	0 .996[c]
Stillbirths	3	100	0	0	1.0 (0.9–1.1)	0.022	–	0 .996 [e]
Preterm Labour	26	83.9	5	16.1	11.5 (4.2–31.5)	<0.001	4.3 (1.4–13.0)	0.011 [d]
Prolonged Labour	41	80.3	10	19.7	18.4 (7.3–46.2)	<0.001	19.0 (7.1–51.1)	0 .000[c]
Assisted Labour	3	100	0	0	1.0 (0.9–1.0)	0.188	–	1.000 [e]
LSCS	48	60	32	40	4.9 (2.7–8.9)	<0.001	4.7 (2.5–8.7)	0.000[c]
Low birthweight	35	85	6	15	15.2 (6.0–38.3)	<0.001	11.2 (4.8–26.3)	0 .000[c]

PIH-Pregnancy induced hypertension.
GDM- Gestational diabetes mellitus.
LSCS-Lower segment caesarean section.
[a] = adjusted for GDM, maternal age and trimester of pregnancy.
[b] = adjusted for PIH LSCS, maternal age and trimester of pregnancy.
[c] = adjusted for GDM and PIH, maternal age and trimester of pregnancy.
[d] = adjusted for GDM and PIH, LBW, maternal age and trimester of pregnancy.
[e] = adjusted for GDM, PIH, PTL, Prolonged labour, maternal age and trimester of pregnancy.

such associations [21,40]. Our findings of positive associations of AADs with PTB and LBW add to this limited equivocal evidence. The incidence of low birthweight in Sri Lanka has remained static for many years [41], likely due to influence of the factors, including AADs, that are not assessed in routine antenatal care program. Any early detection and treatment of AADs may help improve such pregnancy outcome indices.

Miscarriages, stillbirths, and assisted labour occurred exclusively in women with AADs in our study while previous evidence on the association of AADs with such labour outcomes are equivocal [21,34,42,43]. However, the numbers of women with these outcomes in our study was small and precludes making definite conclusions based on them.

The women with AADs in our study predominantly had blood and injection phobia (39.5%, n = 32). This is in contrast to findings of an Indian study [20] and a meta-analysis that included 102 studies [4], where the main domain of AADs was generalized anxiety disorder. This difference observed in the AAD domains may be due to cultural factors the AADs are associated with [4], as well as due to genetic and environmental factors, variations in socio-demographic profiles, personal experiences related to anxiety, ways of expressing anxiety and social influences [10]. As blood and injection phobia is known to be associated with high incidences of PIH, GDM, LSCS, pre-term births and low birthweight [33,37] which may be prevented [44] by various interventions [45], screening for AADs and intervening to mitigate their adverse outcomes need consideration.

Those who were diagnosed with AADs in the current study were referred to the professorial psychiatric unit or the maternal psychiatric unit at CSTH. Accordingly, appropriate management was done on case-by-case basis. The attendance of referral visits of the few who were diagnosed with severe AADs however was unsatisfactory and are unlikely have biased the results in any significant way.

Recognition of adverse maternal and foetal outcomes associated with the AADs would emphasize paying more attention to improve maternal mental health through prevention, early detection, and appropriate management of AADs which is the main strength of this study.

One limitation in our study was not serially repeating assessment of AADs during the pregnancy. As AADs found at recruitment resolving towards the latter part of pregnancy without any intervention is unlikely, any new AADs that developed later in the pregnancy in those who were free of AADs at the time of recruitment could have led to underestimation of the existing associations. Any other systematic misclassification in our study is unlikely. Another limitation in our study is not serially extracting information on new cases (antenatal women) reported with PIH and/or GDM. As this study was an offshoot of a previous validation study, such close follow-up that would be resource intense was not possible. For the same reason, the sample size that was not formally calculated based on the expected outcomes in those with and without AADs may have been too small to detect some outcomes as shown in the statistical analysis section and by our inability to determine associations for infrequent outcomes. However, detection of some associations that the study was underpowered to detect shows the robustness of these observed associations.

Studies conducted elsewhere in the world on AADs and pregnancy outcomes have recommended screening for AADs during pregnancy [3,5] and to commence treatment early. However, screening or intervention for AADs are not routinely performed in Sri Lanka [13]. In the backdrop of our findings, routine screening for AADs in Sri Lankan antenatal women to minimise adverse consequences of untreated AADs is recommended at least as a pilot program.

Further studies with a larger cohort of pregnant women in their first antenatal clinic visit and following up them for anxiety during each trimester of pregnancy and postpartum period will be more valuable to precisely investigate causal associations of AADs and potential adverse pregnancy outcomes. In addition, detection of growth and development of offspring during the early childhood will give additional information on the impact of AADs on the offspring.

5. Conclusions

AADs are strongly associated with PIH, GDM, prolonged labour, LSCS, preterm labour and low birthweight. Exploration of causal pathways of these associations, any interactions with other variables, and effect of any intervention programs are recommended for future research.

Author contribution statement

Manathungei Nirmala Priyadarshanie: Performed the experiments; Analyzed and interpreted the data; Wrote the paper.
Dulshika A. Waas: Analyzed and interpreted the data; Contributed reagents, materials, analysis tools or data; Wrote the paper.
Sampatha Goonewardena: Analyzed and interpreted the data; Wrote the paper.
Sharaine Fernando, Chamara V. Senaratna: Conceived and designed the experiments; Analyzed and interpreted the data; Wrote the paper.

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Data availability statement

Data will be made available on request.

Declaration of interest's statement

The authors declare no conflict of interest.

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Appendix A. Supplementary data

Supplementary data to this article can be found online at 10.1016/j.heliyon.2023.e13900

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