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ABSTRACT Low birthweight (LBW) remains a significant public health problem in Pakistan and further understanding of factors associated with LBW is required. We conducted a hospital-based matched case control study to identify risk factors associated with LBW in a rural district of Pakistan. We found that illiteracy (AOR: 2.68; 95% CI: 1.59 - 4.38), nulliparity (AOR: 1.82; 95% CI: 1.26-2.44), having a previous miscarriage/abortion (AOR: 1.22; 95% CI: 1.06-2.35), having

Introduction

Facteurs associés à une insuffisance pondérale à la naissance dans les cas de grossesses à terme : étude cas-témoins appariés au Pakistan rural

RÉSUMÉ L’insuffisance pondérale à la naissance demeure un problème de santé publique significatif au Pakistan, et une compréhension approfondie des facteurs associés à ce problème est requise. Nous avons conduit une étude cas-témoins appariés en hôpital afin d’identifier les facteurs de risque associés à l’insuffisance pondérale à la naissance dans un district rural du Pakistan. Il est apparu que l’analphabétisme (OR ajusté : 2,68 ; IC de 95 % : 1,59-4,38), la nulliparité (OR ajusté : 1,82 ; IC de 95 % : 1,26-2,44), les antécédents de fausse couche ou d’avortement (OR ajusté : 1,22 ; IC de 95 % : 1,06-2,35), le fait d’avoir eu moins de deux visites de soins prénataux au cours de la dernière grossesse, (OR ajusté : 2,43 ; IC de 95 % : 1,34-2,88), de n’avoir recherché des soins prénataux qu’au troisième trimestre (OR ajusté : 3,62 ; IC de 95 % : 2,14-5,03), de ne pas avoir bénéficié d’une supplémentation en fer et en acide folique pendant la dernière grossesse (OR ajusté : 2,72 ; IC de 95 % : 1,75-3,17), d’avoir souffert d’hypertension durant la dernière grossesse (OR ajusté : 1,42 ; IC de 95 % : 1,13-2,20), d’anémie (OR ajusté : 2,67 ; IC de 95 % : 1,65-5,24) et d’avoir un poids post-partum de moins de 45 kg (OR ajusté : 3,30 ; IC de 95 % : 1,97-4,52) étaient significativement associés à des risques accrus d’avoir un bébé souffrant d’une insuffisance pondérale à la naissance. La présente étude a identifié les facteurs de risque modifiables nécessitant un engagement immédiat des autorités sanitaires.

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Introduction
Low birthweight (LBW) is defined as

Pakistan has one of the highest global burdens of LBW, ranging from 19% in urban areas to 32% in rural areas (8). These high rates contribute towards both the high neonatal mortality and the high stunting rates in children aged

Given that LBW exerts such a high burden of morbidity and mortality further understanding of the associated risk factors is required. The aims of this study were (1) to identify risk factors associated with LBW in term babies in a rural district of Pakistan; and (2) to inform the development of interventions aimed at modifying behaviour and other risk factors for LBW.

Methods

Study design and site

This study was a retrospective, hospital-based, matched case–control study in a rural district of Pakistan. The data were collected between August 2014 and September 2015 from a secondary care hospital (known as THQ KN Shah) located in Taluka (subdistrict) KN Shah of Dadu; a rural district in Sindh Province. This is a 20-bed public hospital with an average of 200 births per month. The hospital has a catchment area of ~150 000 people. The usual length of stay for women at the hospital is about 1 day postpartum.

Sample size

We determined the sample size using the proportion difference approach assuming a confidence level of 95%, power of 80%, case to control ratio of 1:1, detectable odds ratio (OR) of 1.5 and 20% exposure in the control group. A total sample size of 950 (475 cases and 475 controls) was achieved.

Cases and controls

We defined cases as the mothers delivering a live-born singleton baby at term with birthweight 4000 g, those with congenital anomalies, multiple births and preterm births. We matched the cases and controls on the basis of neonatal sex and maternal age on the same day when cases were identified. In the event that there were > 2 eligible controls, 1 was selected randomly.

Data collection

We used a structured and pretested data collection form that was translated into the local language. The data collection from eligible mothers was completed within 24 hours of birth. The data collection form had sections on sociodemographic status and medical and reproductive history of the women. Some data were extracted from the antenatal care (ANC) cards and transcribed onto the data collection form. After completion of the data collection form, the female
The female medical officer also documented women’s postpartum weight with the use of Seca weighing scales. For each woman, 3 readings were taken and the mean weight in kilograms was recorded. The female medical officer also recorded the weight of the neonates soon after birth using Tanita 1584 electronic baby weighing scales. After 3 readings the mean weight in grams was recorded.

### Explanatory variables

The explanatory variables comprised sociodemographic and maternal variables (Table 1). The sociodemographic variables included address of residence and socio-economic status; the latter derived from household assets and utilities score using standard demographic health survey questions. The wealth quintiles were divided into five categories (poorest, poorer, middle, richer and richest). For maternal factors, we collected data on age, education, past reproductive history and information related to the last pregnancy. We recorded age in years, categorized as 30. For maternal education we collected information on number of years of completed schooling and categorized as illiterate (no formal education), primary or less (1–5 years), middle (6–8 years), matric (9–10 years) and intermediate and above (> 10 years). We collected information on parity, defined as the number of previous births and categorized as nulliparous (0), primiparous (1), multiparous (2–4), grand multiparous (≥ 5).

We also collected information on the history of miscarriage, abortion and stillbirth. We sought information about the last pregnancy around the number and timing of the ANC visits; the latter grouped into the following categories 4 visits. The timing of the first ANC visit was documented as having occurs in the 1st, 2nd or 3rd trimester. We also collected the data on the use of iron and folic acid supplementation, calcium supplementation, any history of hypertension and any history of diabetes. The haemoglobin status of the women measured at 1st ANC encounter was also recorded as either anaemic (...

### Data management and statistical analysis

The female medical officer checked the questionnaires for completeness and consistency and coded them before data entry. The Data Management Unit of Aga Khan University, Karachi, Pakistan, entered the data on predesigned data entry screens on Visual Fox Pro software. All data were analysed using SPSS version 19 and conditional logistic regression was used for analysis. Crude and adjusted ORs were used to investigate the factors affecting the incidence of LBW, by bivariate and multiple logistic regression, respectively. We used bivariate analysis to explore the associations between independent variables and LBW, and calculated the crude ORs and confidence intervals (CIs) were calculated. The χ² test was used to test possible bivariate associations between independent variables and LBW. Variables significant at P Ethical clearance
The Ethics Review Committee of Aga Khan University granted approval for the study. The female medical officer explained the study and obtained verbal consent from all participants. The confidentiality of all participants was ensured.

Results

A total of 950 mothers, comprising 475 cases and 475 controls, were included in the study. There were no significant differences in the socioeconomic characteristics or maternal age distribution between the cases and controls (Table 2). However, there were differences in literacy levels, parity, and history of abortion or miscarriage and stillbirth. Cases were less likely to have attended > 4 antenatal visits (17.9 vs 25.9) and to have presented later in pregnancy (23.8% vs 15.6%). The use of calcium supplementation during the last pregnancy was low (14.8% and 13.9%) among the cases and controls, respectively. The use of iron and folic acid supplementation was higher in the controls (46.4%) compared to cases (25.7%). Anaemia status based on low haemoglobin concentration (Table 3).

Univariate analysis was performed to determine the association between maternal risk factors and LBW (Table 3). The analysis revealed that illiteracy (OR 2.9, 95% CI 1.74–4.88), nulliparity (OR 1.77, 95% CI 1.19–2.63), previous miscarriage or abortion (OR 1.15, 95% CI 1.14–2.28),

In multivariable analysis all these factors remained significant (Table 4). Illiteracy (AOR 2.68, 95% CI 1.59–4.38), nulliparity (AOR 1.82, 95% CI 1.26–2.44), previous miscarriage or abortion (AOR 1.22, 95% CI 1.06–2.35).

Discussion

This study identified a range of modifiable factors related to LBW in term babies in a rural region of Pakistan. These factors included illiteracy, nulliparity, previous miscarriage or abortion, number and timing of ANC visits, lack of iron and folic acid supplementation during pregnancy, presence of hypertension or anaemia during pregnancy and postpartum maternal weight.

Previous research has documented that educated women are less likely to have an LBW baby and maternal education has a 33% protective effect against LBW (14). This has been observed in similar low-resource settings such as Nepal (15) and Bangladesh (16), and in a previous study from Pakistan (17). We also found that illiteracy was associated with LBW delivery, which is likely related to reduced service utilization and less knowledge of positive health behaviour (18). Improving attendance and access to education by young girls will address this issue, although any effect will require a long lead time and long-term investment that ensures maximum enrolment and continuation of the girls in school. Increasing health literacy among illiterate women is complex and requires additional resources directed toward individual counselling (18).
We found that nulliparous mothers were more likely to deliver LBW babies compared to multiparous women. This finding is in agreement with previous meta-analyses (19) showing that nulliparous women are consistently more likely to have LBW babies compared to their multiparous and grand multiparous counterparts. Several hypotheses have been put forward to explain this association, including the biological immaturity of young mothers and maternal–fetal competition for nutrients in women still trying to achieve their own growth potential (20,21). Recent estimates by the United Nations Children’s Fund (UNICEF) revealed that 21% of the girls in Pakistan are married before the age of 18 years (22). Throughout the country this has changed from 16 years in 1960 to 22 years in 2015 (23) but the mean age for marriage in rural areas remains around 16–18 years (8). Primary reasons for this early age of marriage in Pakistan are connected with tradition, social and gender inequality and lack of awareness of the harmful impact of early marriages (24). Pakistan’s Child Marriage Restraint Act 1929 sets the legal age for marriage to 16 years for women and 18 years for men. While preliminary efforts are being made to increase the minimum age for women to 18 years, this has not yet been enacted (25). Greater political will and public education are required to address the issue of early marriage and childbearing, along with greater access to modern methods of contraception.

In our study, a previous history of abortion or miscarriage was significantly associated with increased odds of delivering LBW infants. This was in agreement with previous studies (26,27) and a systematic review (28) that showed a significant relationship between miscarriage and abortion and LBW; the risk of LBW appears to increase with increasing number of previous abortions (29). The underlying biological mechanisms responsible for this association may be cervical insufficiency as a result of damage caused by stretching of the cervical canal through dilatation and curettage, and cervical and uterine adhesions as a result of post abortion complications (30,31). Also, miscarriages can lead to cervical incompetence and uterine abnormalities resulting in intrauterine growth restriction, which subsequently causes LBW (32). In Pakistan the burden of abortion and miscarriage is high, which was reported as 12% and 1.7%, respectively, in the recent Pakistan Demographic and Health Survey (PDHS) (8). Another study conducted in 2014 estimated that annually about 2.25 million abortions are conducted in Pakistan leading to a national abortion rate of 50 per 1000 women (15–49 years) (33). Averting miscarriages and abortions requires extra vigilance during ANC and greater access to more reliable contraceptive methods. However, the prevalence of using the most effective methods, including intrauterine devices and implants, is only 3% in Pakistan (8), which is well below the neighbouring countries.

Adequate and timely antenatal care is of paramount importance for pregnant women and improves pregnancy outcomes. Studies consistent with our findings from similar settings to Pakistan have demonstrated an increased risk of delivering an LBW baby with delayed initiation of ANC, with reduced ANC visits and with inadequate service provision during ANC (34–36). We reported similar results and showed that the odds of delivering an LBW baby were greater in
women who had fewer than the recommended minimum 4 ANC visits and started ANC late in their pregnancy. The recent PDHS showed that 37% of pregnant women had ≥ 4 ANC visits with a median 3.7 months duration of pregnancy at first ANC encounter. However in rural areas only 26% had ≥ 4 ANC visits and the median gestation at booking was 4.3 months (8). Given this and the acknowledged importance of ANC it is reasonable to call for reforms to the maternal neonatal and child health policy to ensure that ANC is delivered to all pregnant women as per the WHO guidance and recommendations.

Studies have demonstrated that non-use of iron supplements and maternal anaemia during pregnancy have a negative effect on birthweight (37, 38). In our study, maternal anaemia and non-use of iron supplementation during pregnancy were independently significantly associated with increased risk of LBW. A seminal study conducted in 2001 explored the potential mechanisms of the association between anaemia and LBW and concluded that anaemia can induce maternal and fetal stress, which stimulates the release of corticotropin releasing hormone. In turn, this increases fetal cortisol production, which consequently inhibits longitudinal growth of the fetus (39). Pakistan has a high anaemia burden and use of iron supplementation among pregnant women is alarmingly low (45%) (8). To reduce the burden of anaemia among women, efforts should be made to increase the use of iron and folic acid supplementation, and the best strategies are iron supplementation and food fortification (40).

In our study postpartum weight

Similarly, hypertension was significantly associated with LBW in our study, which is supported by previous research (44,45). It is believed that hypertension causes a decrease in uteroplacental blood flow, which results in LBW and other complications (46). Data from Pakistan have reported a 15% frequency of hypertensive disorders during pregnancy (47). Therefore, early detection and management of gestational hypertension is imperative. To achieve this target in Pakistan, first-line healthcare workers should be trained and encouraged to manage hypertension in community settings using the WHO recommended guidelines (48).

We used a matched case–control design to explore the risk factors for LBW, which was an acceptable design for an analytical risk factor study. However our study had some limitations. First, we used the postpartum maternal weight as a proxy indicator for maternal BMI so our finding of the association between maternal underweight and LBW should be viewed with caution. Second, this study was carried out in a rural hospital of Sindh Province, therefore, the findings cannot be generalized to the whole country. Third, the retrospective nature and use of hospital records might have introduced recall bias.
In conclusion, we identified important risk factors associated with LBW, which are all modifiable with little investment and commitment. Therefore, a holistic approach is required from government institutions, nongovernmental organizations and civil society to ensure: proper education and counselling for women; legislation for the revised age of marriage; provision of timely and adequate ANC; universal coverage of iron and folic acid supplementation during pregnancy; and an improved family planning programme with long-acting reversible contraceptives as key options.

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