Birth weight centiles and small for gestational age (SGA) by sex and ethnicity for England and Wales.

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Contributors

AFS drafted the paper and supervised the statistical analysis conducted by PA. All the authors provided intellectual input, interpreted the results, and helped to revise the manuscript. All authors approved the final version of the manuscript and agreed to be accountable for all the aspects of the work in ensuring that questions related to the accuracy or integrity of any part of the work are appropriately investigated and resolved. AFS is the guarantor of this paper.

Competing Interests None declared.

Ethics and Information Governance statement

This study uses SAHSU data, covered by national research ethics approval from the London-South East National Research Ethics Committee - reference 17/LO/0846. Data access is covered by the Health Research Authority - Confidentiality Advisory Group under section 251 of the National Health Service Act 2006 and the Health Service (Control of Patient Information) Regulations 2002 HRA CAG reference: 14/CAG/1039. Identifiable information has only been used under strict data sharing agreements with the data providers. SAHSU does not have permission to supply data to third parties.

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ABSTRACT

Objectives To construct UK Ethnic Birth Weight Centiles (UK-EBWC) for gestational age and cut-offs for small for gestational age (SGA) for England and Wales and to evaluate the SGA misclassification using the UK centiles.

Design Analysis of national birth data.

Participants All live singleton births in England and Wales in 2006 to 2012, as recorded by the Office for National Statistics (ONS) and birth registrations, linked with National Health Service (NHS) into Numbers for Babies (NN4B).

Main Outcome Measures Both sex-specific and ethnicity-sex-specific birth weight centiles for gestational age, and ethnicity-sex-specific SGA cut-offs. Centiles were computed using the Generalized Additive Model for Location, Scale and Shape (GAMLSS).

Results Our sex-specific centiles performed well and showed an agreement between the expected and observed number of births below the centiles. The ethnicity-sex-specific centiles for Black and Asian presented lower values compared to the White centiles. Comparisons of sex-specific and ethnicity-sex-specific centiles shows that use of sex-specific centiles increases the SGA diagnosed cases by 50% for Asian, 30% for South Asian (Indian, Pakistani and Bangladeshi) and 20% for Black ethnicity.

Conclusions The centiles show important differences between ethnic groups, in particular the 10^{th} centile used to define SGA. To account for these differences and to minimize misclassification of SGA, we recommend the use of customized birth weight centiles .

Keywords: Birth weight, Ethnicity, Small for gestational age, birth weight centiles, UK charts

What is already known on this topic?

- Identifying babies who are small for gestational age (SGA) helps identify growth-restricted newborns who may be at risk of immediate and long-term morbidity.
- Some ethnic minority groups are characterized by lower birth weights as compared to white ethnicity.
- Currently available birth weight centiles for the UK are sex-specific only, and do not reflect potential (constitutional) differences throughout gestation by ethnicity

What this study adds

- This study provides ethnicity-sex-specific birth weight centiles derived from national birth records in 2006-12 in England and Wales for 4,927,889 births.
- Produces centiles and cut-offs that can be used in epidemiological studies and inform clinical practice.
- Ethnic-specific centiles and thresholds may avoid misclassifying ethnic minority babies (particularly South Asians) as SGA and subsequently reduce unnecessary interventions, organizational (hospital) costs and parental anxiety.

INTRODUCTION

Birth weight is an important indicator for fetal growth and neonatal health in both clinical and perinatal research . Low birth weight (<=2500 g) and very low birth weight (<1500 g) predict possible future morbidity, but these measures do not distinguish between small babies born early and small babies who grew poorly in utero. Small for gestational age (SGA), defined as a birth weight below the 10th centile for gestational age, is a commonly used measure which adjusts birth weight for gestational age and helps improve the identification of poor growth in utero in both clinical practice and epidemiological research.

In 2009, new UK-WHO growth charts for children aged 0-4 years (1) were developed by the Royal College of Paediatrics and Child Health, which replaced other existing population birth weight centile charts in the United Kingdom (2-4). In 2011, revised birth centiles were released using data from five studies from 1983-1993(5), with less than 10,000 births of which over 80% were from the East of England (around Cambridge).

Updated UK birth weight centiles were published in 2017 by the MBRRACE programme (Mothers and Babies: Reducing Risk through Audits and Confidential Enquiries across the UK (Norris, Seaton et al. 2017). Centile were constructed using ~1.3 million birth records for 2013-14 from the National Health Service (NHS) numbers for babies (NN4B), with centiles being higher than UK-WHO. However, these updated centiles did not account for ethnicity, whereas evidence has shown that ethnic-specific birth weight charts have improved prediction of neonatal morbidity and mortality (6, 7).

The UK Millennium Cohort Study (8) found that birth weight distributions differ by ethnic group with White new-borns being heavier than Black and Asians. Differences in birth weight for Black and Asians (Pakistani and Bangladeshi) were explained by socio economic factors, but for Indian and Bangladeshi infants differences were associated with maternal and infant factors. That South Asian ethnicity babies have lower birth weight has been observed in other studies conducted in Canada and Netherlands (9, 10). There is evidence (11-13) that the observed South Asians lower birth weight is explained by the physiological characteristics, rather than pathological reasons. In this perspective, several researchers (14-18) recommend the use of customized charts to reduce antenatal care by improving the distinction between physiological and pathological variation in new-borns birth weight.

In UK, ethnic birth weight centiles for ethnic minorities living are based on small and outdated data, and may not be representative of the current South Asian/Pakistani population (19). In addition, due to the lack of ethnic-specific centiles researchers rely on birth weight centiles from other countries or calculate centiles within their own study population to specify SGA (20, 21).

In this study, we provide the sex-specific and ethnicity-sex-specific birth weight centiles (UK-EBWC) for white, Black and Asian and South Asian ethnicity births, including the cut-offs for the 10^{th} centile used to define SGA, based on over 4 million records from England and Wales.

METHODS

Data

We included all live singleton births in England and Wales from January 1st, 2006 to December 31st, 2012 using data from the ONS (Office National Statistics) Birth Registrations and NHS Numbers for Babies project (NN4B). The two datasets were linked to produce an enhanced birth registrations to include gestational age and ethnicity from NN4B, with 99.8% of NN4B records linked with a registration record using the NHS number (22). The final dataset includes: the year of birth, sex, birth weight, gestational age in completed weeks, and baby's ethnicity (as reported by the mother).

Data cleaning

The analysis was restricted to singleton live births occurring between 24 and 42 weeks' gestation. In the data cleaning process, we removed multiple births, implausible birth weight gestational age combinations, missed ethnicity (supplementary material Figure 1). We then split the births into four ethnic groups (supplementary material table 1): White, Asian, Black and Other, to investigate variation in birth weight. Additionally, we split Asians into South Asians (Indian, Pakistani and Bangladeshi) and other Asians (any other Asian background) to examine whether South Asians require separate birth weight reference values from all Asians (19). For each subset defined by ethnicity, sex and gestational age, we excluded birth weight outliers using Tukey fences. Tukey fences is a robust method as it makes no distributional assumptions (23), the lower cut-off is defined as the first quartile minus twice the inter-quartile range (2IQR) and the upper cut-off is the third quartile plus 2 IQR. We removed these outliers separately for the sex-specific charts and for the ethnic group specific charts, for the latter we removed outliers after splitting (table 1) by ethnic group (White, Asian and Black). We excluded the 'Other' ethnic group (6.9% of births) from

the analysis as it does not represent a meaningful homogeneous group for analysis and excluded births with missing ethnicity information.

Statistical Analysis

We computed summary statistics and outlined the density plot for each sex and ethnicity-sex subsets. For each of these subsets, to estimate birth weight charts we used the Lambda-Mu-Sigma (LMS) that models mean, standard deviation, skewness. As we observed kurtosis in the data, we also fitted a second model, the Box-Cox Power Exponential (BCPE) using Generalized Additive Model for Location, Scale, and Shape (GAMLSS) (24). The BCPE is similar to LMS, but additionally models kurtosis as a fourth parameter. We compared the two fits: at extremes centiles (1% and 99%), where they could possible diverge, and using a measure of the model quality (generalized Akaike Information Criterion (GAIC)). Both methods showed that BCPE presented a better fit, so we used this for our analyses. Based on GAMLSS output, we computed birth weight centiles used in clinical practice, rounded to 0.4^{th}, 2^{nd}, 9^{th} , 25^{th}, 50^{th}, 75^{th}, 91^{st}, 98^{th}, 99.6^{th}. The centiles are all two-thirds of an SD (standard deviation) scores apart, as reported by (25). We also included the 10^{th} centile, mostly used to define small for gestational age.

Goodness of fit and comparison

To verify that the centiles performed well, we computed the observed and expected proportion of births below a given centile and checked if they were in agreement.

Small for gestational age and misclassification rate

We conducted a graphical inspection of the ethnic group specific and sex-specific curves to look at distributional form, and then assessed the ethnic-sex-specific SGA misclassification using sex-specific centiles for Asian and Black, South Asian and Other Asian. All analyses were conducted in R and using the GAMLSS package (24).

Patient involvement

Patients were not involved in the development of the research question or the design and conducting of the study.

RESULTS

Descriptive Results

There were 4,081,910 live singleton births in 2006-12, with 94 % of births observed between 37 - 42 weeks. White ethnicity was the most common ethnicity for 74% of all births, with smaller proportions of Asian, Black or Other births. White babies were heaviest followed by Black, Other Asian, South Asian. Males were heavier on average than females, between 2.7% (Other Asians) to 3.6% (White) (Table 1). In figure 1, the density plots for both females and males show that white and sex-specific (all data) are overlapping, while Asian and Black are shifted downwards, this also persist at different centiles levels and gestation weeks (Figure 2).

Performance of centiles

We report the performance of our sex-specific centiles by comparing the observed vs expected percentage of births below centiles. For the 2nd centile we classified males at 2.03% and females

at 2.05% versus an expected average of 2.28%, and at the 98th centiles 2.62% and 2.22% for males and females respectively (Table 2 and supplementary Table 2).

Small for gestational age and misclassification rate

We compared our ethnic-sex-specific 10th centiles for white, Asian and Black against our sex-specific centiles (see Figure 3). White male and female centiles were close to the sex-specific centiles, whereas differences were seen for Black and Asian centiles. Black ethnicity centiles were 80g and 52g lower (on average across all gestational weeks) for male and female births respectively compared to sex-specific centiles (Figures 3, supplementary Table 3). For Asian males were 113g and females 101g were lower and similarly for South Asian males 122g and for females 106g lower (supplementary figure 2 and 3).

Within Asian, South Asian and Other Asian, the largest difference was between Asian and Other Asian births with Asian males heavier by 56g than Other Asian births and females 35g lower for Other Asian births than Asians (on average across all gestational weeks). The birth weight of the 10th centile for South Asians was the lowest among Asians, especially after 32 weeks. Using sex-specific centiles to assess SGA rather than the ethnic-specific centiles (supplementary table 4), we found that for Asian and South Asian births the percentage of births classified as SGA increased by 50%, whereas for Other Asian and Black there was an increase of 30% and 20%, respectively.

DISCUSSION

We provide sex- and ethnic-specific birth weight centiles)for England and Wales (UK-EBWC) based on a large national births' dataset. These new centiles provide a tool to help assess fetal growth, ethnic-specific centiles and small for gestational age births.

Our sex-specific centiles using the UK-EBWC data for 2006-12 for all live singleton births were similar matching to those published from the MBRRACE group (data not shown) (25), who also used data from NN4B (but for 2013-14) plus stillbirths alive at onset of labor (n=1,269,403). Both MBRRACE and our study centiles showed higher birth weights than those reported in 2009 UK-WHO charts (5), in line with observed increased birth weight trends between 2006-2012 as reported in Ghosh (26). The UK-WHO revised charts computed on 9443 births, mostly from East of England (5), were limited and not representative.

These two most recent published sex-specific birth weight centiles for the UK have limitations if used to assess Black and Asian births. Whereas, we were not able to directly compare the percentage of misclassification that would have occurred using the MBRRACE data, given our sex-specific curves were similar to the MBRRACE curves, it is likely that using them will lead to similarly increased counts of SGA cases.

The level of misclassification seen for South Asian births in our study is comparable to that seen in a study conducted in Canada (10) and a study Siri Lanka comparing but using Bangladeshi and European centiles. Maso et al. (27) also demonstrated that only SGA cases identified with a ethnicity based charts were at a risk of actual adverse outcome. Narchi et al. (28) suggested that

relying on a general population based charts will fail to identify a portion of SGA cases that need actual postnatal care.

Whether the differences in birth weight distribution and mis-classification in SGA diagnosis are imputable to physiological or pathological reasons has been debated (29-31).

These differences in birth weights in ethnic minorities have been observed to be consistent also between immigrant mothers for South Asian and Black in UK when compared to second generations, suggesting differences may be physiological (32-34).

Nevertheless, other studies have reported ethnic differences in birth weight for gestational age even after adjusting for all plausible maternal characteristics at the population level (6, 7). Sex-specific birth weight charts such as the UK-WHO and MBRRACE charts imply that one chart fits all babies irrespective of ethnicity. However if ignored, the observed ethnic differences in birth weight reference values increase the misclassification of babies of ethnic minorities as SGA, and this could increase further as changes occur in the population composition (35).

Both the UK-WHO (5) and MBRRACE (Norris, Seaton et al. 2017) present 9^{th} centiles and not 10^{th}. The choice to focus on the 10^{th} centile is because most of the studies, used this value as a threshold for SGA case. While we do not expect major difference between the 9^{th} and 10^{th} centiles, the observed discrepancies observed in figure 3 would persists.

Compared to the updated UK centiles (MBRRACE), the results presented here have the advantage of a larger dataset comprising over four million live singleton births. Also, the NN4B data are collected nationally rather than from a specific region (5) or hospital population as used for the

UK-WHO charts. For each ethnic group and gestational age we had enough observations to compute robust centiles. Our analysis highlights that each ethnic specific curve has its own functional form that supports the need for ethnic-specific centiles.

One of the limitations is that our birth weight reference values were computed without any information on maternal medical conditions during pregnancy. Typically, complicated births are excluded in other studies when constructing reference birth weight charts. It is unknown to what extent this may have influenced our ethnic-specific birth weight reference values. Because of this, the Royal College of Obstetrics and Gynaecologists recommend birth weight charts customized for maternal measures that influence birth weight for clinical use to improve the prediction of adverse neonatal outcomes. However, most population birth weight charts used as a reference for defining SGA births, in epidemiological studies do not hold maternal measures, because these were usually not available on population birth registries (36).

The second limitation is our choice of ethnic groups. We chose three main ethnic groups as this grouping is often used in epidemiological studies (20, 21), but these three groups comprise subgroups with many cultural and genetic differences. SGA is often used in environmental epidemiological studies as a binary outcome to detect possible exposure effects on fetal growth. Using centiles including all ethnicities does not fit all births and may lead into an incorrect number of SGA cases especially for specific ethnic groups. Finer ethnic grouping may have shown additional difference between groups as it has been shown that birth weights may differ even within the same ethnic groups (37, 38), but more categories would have led to smaller sample sizes and less stable estimates, in particular at lower gestational ages.

A third limitation is associated with the information on the babies' ethnicity registered in the NN4B data. Ethnicity of the baby is reported by the mother and while the classification of white or non-white births seems to be consistent between self-reported and health databases, specific minority groups may be misclassified depending on how the mother defines ethnicity (39).

Finally, given that birth weight trends are known to change over time(26), we recommend that such analyses are updated periodically.

Conclusions

In conclusion, we compiled birth weight centile charts based on over 4 million live singleton births for the main ethnic groups in England and Wales, including the 10th centiles for defining small for gestational age. Using sex only centiles that do not also take account of ethnicity can lead to SGA misclassification. National reference birth weight charts should account for ethnic group to better represent the diverse population of England and Wales. The centiles can be used by researchers to determine SGA by ethnic group to avoid the misclassification of babies born small or large for gestational age, which may be particularly useful in epidemiological studies.

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Tables and Figures:

Table 1: Distribution by ethnicity and sex of live singleton births between 24 and 42 weeks' gestational age, by number and percentage after removing outliers. Number of observations (n) after outlier's removal, and percentage (%), mean and standard deviation of birth weight by sex and ethnicity for eligible births in UK-EBWC from 2006-2012.

Ethnicity	White		Black		Asian		South Asian[1]		Other Asian[1]	
Sex	Male	Female	Male	Female	Male	Female	Male	Female	Male	Female
n	1,735,148	1,643,808	119,741	116,781	229,423	219,680	193,660	185,752	35,770	33,961
%	74.99	74.42	5.18	5.31	9.92	9.99	8.37	8.44	1.55	1.54
Mean birth weight (g)	3470	3345	3342	3221	3186	3094	3171	3079	3269	3181
Standard deviation (g)	562	533	580	566	533	509	532	508	532	508
Sex difference (g)	125		121		92		92		88	

1 South Asian (Indian, Pakistani and Bangladeshi) and other Asian (any other Asian background) are two subsets derived from Asian.

Table 2: Observed and expected percentages below selected centiles by sex.

	Expected	Males	Risk Difference	Females	Risk Difference
0.4th	0.38	0.44	0.06	0.46	0.08
2nd	2.28	2.03	-0.25	2.05	-0.23
9th	9.13	8.76	-0.37	8.76	-0.37
10th	10	9.81	-0.19	9.70	-0.30
25th	25.24	24.76	-0.48	24.72	-0.52
50th	50	50.29	0.29	49.81	-0.19
75th	74.76	75.34	0.58	74.91	0.15
91st	90.67	90.96	0.29	90.81	0.14
98th	97.72	97.83	0.11	97.78	0.06
99.6th	99.62	99.60	-0.02	99.61	-0.01

Figure 1: UK-EBWC 2006-12 birth weight centiles distribution for White, Black and Asian births compared with UK-EBWC, by sex.

Figure 2: UK-EBWC birth weight centiles for White, Black and Asian births compared with UK-EBWC sex-specific.

Figure 3 UK-EBWC birth weight 10^{th} centiles for ethnic-specific males compared with the sex-specific centile.