**A Cross-Sectional Study of the Relationship Between Black Ethnicity and Meconium-Stained Amniotic Fluid in Labouring Women of Urban Western Europe**

**Word Count:**

**1491**

**Introduction**

Foetal delivery with meconium-stained amniotic fluid (MSAF) can be a sign of normal foetal gastrointestinal maturation, though it may also indicate foetal compromise resulting in poor outcomes for the neonate. Identifying high-risk groups could help with resource allocation, preparation, and education. To analyze the association between black ethnicity and MSAF, a cross sectional study was conducted, collecting healthcare records from 16,490 labouring mothers in urban areas of Western Europe during the early 2000’s by attending midwives which included data on other potential confounders including: maternal age, epidural use, pyrexia, body mass index (BMI) scores, whether or not the baby was in breech position, nulliparity, multiple births, abnormal foetal heart rate, smoking habits, labour duration, and late-term births.

**Methods**

All statistical analysis was conducted with Stata 17. The primary exposure of interest was black ethnicity and the outcome was meconium-stained amniotic fluid (MSAF).

Three observations were missing data, all of which were from BMI. There was insufficient statistical power to assess differences in characteristics between individuals with and without missing data, and as these observations constitute 0.02% of the sample, and could thus not significantly affect estimates, they were dropped from future analysis as BMI proved to be an important variable. 16,482 observations remained after dropping missing observations.

The categorical variables age and BMI were grouped into significant categories. Four bins were created for age, <20, 20-26, 27-34, and >34 years old. 13 to 19 is commonly used as the lowest age category in pregnancy studies and 35+ years is considered advanced maternal age. The remaining age range, 20 to 34, was evenly split by years. Age bin <20 was set as baseline. BMI was split into five bins as recognized by the Centers of Disease Control (CDC): underweight (<18.5), normal (18.5-24.9), overweight (25-29.9), obese (30-34.9), and extremely obese (>35). Normal BMI was set as baseline.

Pearson’s chi-squared test was utilized to calculate crude association p-values between all variables and MSAF as well as to calculate any association between the primary exposure and the remaining independent variables. Unadjusted odds ratios (OR) and 95% confidence intervals (c.i.) were calculated with Mantel–Haenszel (MH) tests for each variable to the outcome independently. Spearman test of correlation was used to assess multicollinearity.

Effect modification was assessed by comparing logistic model fit with and without an interaction factor between ethnicity and each variable independently via likelihood ratio tests (LRTs). Variables with significant interaction were then tested against models with only ethnicity to assess model fit and significance of the interaction terms.

A test for trend was conducted for non-binary variables to assess inter-stratum estimate variation, assuming linear trend as the null hypothesis.

Individually adjusted ORs and 95% c.i.s were calculated for each variable that was significantly associated to the outcome and primary exposure, or that significantly modified the exposure with logistic regressions (LRs).

The final LR model fit the significant confounders and effect modifiers, and stratified results via linear combinations of parameters (lincom) are reported.

**Results**

There were 12,274 (74.5%) white/other ethnicity women and 4,208 (25.5%) black women. 13,176 (79.9%) women did not have meconium-stained amniotic fluid, and 3,309 (20.1%) did. 19.3% (2,372) of white/other women had MSAF as did 22.3% (937) of black women.

All variables aside from smoking and age category were significantly associated to the outcome (Table 1).

Unadjusted MH analysis reveals that black women are 1.20 (c.i. 1.10 to 1.30, p < 0.001) times as likely to have MSAF as white/other ethnicities (table 1).

Smoking and age category will be dropped from adjusted analyses as they have insignificant measures of effect and p-values.

Spearman correlation found no evidence of multicollinearity, suggesting all variables explain different variation in the data.

Ethnic category is strongly associated to BMI (p < 0.001), nulliparity (p = 0.001), abnormal foetal heart rate during labour (p < 0.001), and late-term birth (p < 0.001), all of which are also significantly associated to the outcome, suggesting these variables may act as confounders. Epidural use, pyrexia, baby in breech position, multiple birth, and labour duration were not significantly associated to the exposure of interest.

LRTs to assess effect modification found significant interaction between ethnicity and nulliparity (p = 0.03), abnormal foetal heart rate during labour (p < 0.001), and late-term birth (p = 0.003). All three individual models with interaction terms were then tested against a model with just ethnicity, and all significantly improved model fit (p < 0.001).

After individually adjusting for BMI, nulliparity, and late-term birth, there remains a significant association between ethnicity and MSAF (Table 2). However, after adjusting for abnormal foetal heart rate during labour, this association is diminished (OR 0.89, c.i. 0.79 to 1.01, p = 0.065). Both late-term birth and nulliparity significantly change the estimate of effect, but BMI does not (Table 2).

The final logistic model was fit with ethnicity, BMI, and interaction terms between ethnicity and nulliparity, abnormal foetal heart rate during labour, and late-term birth. The final adjusted OR between black ethnicity and MSAF is 0.94 (0.80, 1.10) with a 95% c.i. that overlaps 1.00, and is insignificant (p = 0.421).

The effect of nulliparity on MSAF was significant in white/other ethnic groups (p = 0.007), with nulliparous women having 1.15 (c.i. 1.03 to 1.26) times the odds as mothers who had previously given birth, though there was no significant effect of nulliparity in black women (p = 0.630). Nulliparous black women were significantly less likely (p = 0.010) to have meconium-stained amniotic fluid than white/other women, with 0.79 (c.i. 0.65 to 0.94) times the odds.

Late-term pregnancies resulted in 1.61 (c.i. 1.45 to 1.78) times the odds of meconium-stained amniotic fluid (p < 0.001) in white women, and 2.24 (c.i. 1.83 to 2.75) times the odds in black women (p < 0.001). Late-term black women were 1.31 (c.i. 1.05 to 1.64) times as likely as late-term white women to have MSAF (p = 0.018).

Abnormal foetal heart rate (FHR) resulted in 6.10 (c.i. 5.48 to 6.76) times the odds of MSAF in white women (p < 0.001) and 10.67 (c.i. 8.97 to 12.69) times the odds in black women (p < 0.001). Black women with abnormal FHR were 1.64 (c.i. 1.35 to 2.00) times as likely as white women to have MSAF (p < 0.001).

As BMI does not interact with ethnic group and there is no there is no difference in the goodness of fit between models assuming linear trend and models estimating separate effects (p = 0.138), the effects of BMI can be assumed to be linear. Overall, BMI has an OR of 1.20 (c.i. 1.10, 1.31, p < 0.001), though stratum specific rates are given in table 3.

**Discussion**

Crude analysis suggested a significant (p < 0.001) 1.20 (c.i. 1.10 to 1.30) times chance that black women have MSAF compared to white/other ethnicities. The final logistic model indicates that black women are 0.94 (c.i. 0.80 to 1.10) times as likely with an insignificant association between ethnicity and MSAF (p = 0.421). Epidural use, pyrexia, baby in breech position, multiple birth, and labour duration were excluded from the final regression as all were associated to the outcome, but not to ethnicity, and were thus not likely to confound that association. The insignificant variables smoking and age category were also dropped. BMI, nulliparity, abnormal foetal heart rate during labour, and late-term birth were all significantly associated to both exposure and outcome suggesting they might confound the relationship. Individually adjusted analysis revealed that all variables but BMI altered the crude OR estimate and 95% confidence interval, however BMI was still included in the final model with estimates stratified because while there was only slight evidence of a non-linear trend (p = 0.138), the stratum-specific estimates varied seemingly drastically. There was strong evidence (p < 0.001) of interaction between late-term birth and ethnicity (table 3), with late-term black women being 1.31 (c.i. 1.05 to 1.64) times as likely as late-term white women to have MSAF (p = 0.018). There was also strong evidence of interaction between ethnicity and abnormal foetal heart rate (FHR) and nulliparity.

The greatest impact on the crude measure of effect was adjusting for abnormal FHR, which is also the variable that imposes the greatest risk factor for MSAF.

Limitations:

There are several ways by which information bias may have been introduced. It is not clear whether or not there was a standardized method of assessing meconium-staining; differential measuring techniques could introduce information bias. Additionally, BMI does not account for fat to muscle ratios and distributions or metabolic health, so it may be a fundamentally flawed measurement. Lastly, as smoking was assessed retrospectively, patients could provide inaccurate data.

The generalizability of these results is also questionable as only urban mothers of Western Europe were selected, potentially introducing selection bias if the results were to be disseminated for use in rural parts of Western Europe or other parts of the world.

Unmeasured confounding such as preeclampsia, diabetes, hypertension, and any other unmeasured variables may also limit these findings.

Table 1: Crude OR, 95% c.i., and p-values between each variable and MSAF

|  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- |
| Variable | Categories | Meconium (+) | Meconium (-) | OR (95% c.i.) | p-value |
| Age category | 13-19 | 153 (18.1%) | 694 (81.9%) | 1.00 (Reference) | 0.079 |
|  | 20-26 | 1038 (19.8%) | 4217 (80.2%) | 1.12 (0.93, 1.35) |  |
|  | 27-34 | 1677 (20.0%) | 6692 (80.0%) | 1.14 (0.95, 1.37) |  |
|  | 35+ | 441 (22.0%) | 1570 (78.0%) | 1.27 (1.04, 1.56) |  |
| Epidural use | No | 2262 (17.7%) | 10555 (82.3%) | 1.00 (Reference) | <0.001 |
|  | Yes | 1047 (28.6%) | 2618 (71.4%) | 1.87 (1.71, 2.03) |  |
| Pyrexia | No | 3244 (20.0%) | 13053 (80.0%) | 1.00 (Reference) | <0.001 |
|  | Yes | 65 (35.1%) | 120 (64.9%) | 2.18 (1.61, 2.95) |  |
| Ethnicity | White/other | 2372 (19.3%) | 9902 (80.7%) | 1.00 (Reference) | <0.001 |
|  | Black | 937 (22.3%) | 3271 (77.7%) | 1.20 (1.10, 1.30) |  |
| Baby in Breech Position | No | 3197 (19.8%) | 12973 (80.2%) | 1.00 (Reference) | <0.001 |
|  | Yes | 112 (35.9%) | 200 (64.2%) | 2.27 (1.80, 2.87) |  |
| BMI | <18.5 | 81 (14.1%) | 495 (85.9%) | 0.71 (0.56, 1.15) | <0.001 |
|  | <24 | 1968 (18.8%) | 8506 (81.2%) | 1.00 (Reference) |  |
|  | 25-29 | 882 (22.5%) | 3032 (77.5%) | 1.26 (1.15, 1.38) |  |
|  | 30-34 | 278 (24.8%) | 884 (75.2%) | 1.42 (1.23, 1.64) |  |
|  | >35 | 100 (25.3%) | 296 (74.7%) | 1.46 (1.16, 1.84) |  |
| Nulliparity | No | 1619 (17.3%) | 7745 (82.7%) | 1.00 (Reference) | <0.001 |
|  | Yes | 1690 (23.7%) | 5428 (76.3%) | 1.49 (1.38, 1.61) |  |
| Multiple birth | No | 3279 (20.3%) | 12896 (79.3%) | 1.00 (Reference) | <0.001 |
|  | Yes | 30 (9.8%) | 277 (90.2%) | 0.43 (0.29, 0.62) |  |
| Abnormal foetal heart rate during labour | No | 1662 (12.5%) | 11625 (87.5%) | 1.00 (Reference) | <0.001 |
|  | Yes | 1647 (51.2%) | 1548 (48.8%) | 7.44 (6.83, 8.11) |  |
| Smoking | No | 2652 (19.9%) | 10704 (80.1%) | 1.00 (Reference) | 0.145 |
|  | Yes | 657 (21.0%) | 2469 (79.0%) | 1.07 (0.98, 1.18) |  |
| Labour duration | <4 hours | 603 (15.0%) | 3411 (85.0%) | 1.00 (Reference) | <0.001 |
|  | 4-6 hours | 850 (17.4%) | 4039 (82.6%) | 1.90 (1.06, 1.33) |  |
|  | 7-9 hours | 706 (20.6%) | 2726 (79.4%) | 1.47 (1.30, 1.65) |  |
|  | >10 hours | 1150 (27.8%) | 2997 (72.2%) | 2.17 (1.94, 2.42) |  |
| Late-term birth | No | 2261 (17.7%) | 10520 (82.3%) | 1.00 (Reference) | <0.001 |
|  | Yes | 1048 (28.3%) | 2653 (71.7%) | 1.84 (1.69, 2.00) |  |

Table 1: Variable composition breakdown by strata, Mantel–Haenszel ORs and 95% c.i.s, and chi-squared p-values of association to outcome.

Table 2: Individually adjusted ORs, c.i.s, and p-values between ethnic group and MSAF

|  |  |  |
| --- | --- | --- |
|  | OR (95% c.i.) | P-value |
| Unadjusted effect of black ethnicity | 1.20 (1.10, 1.30) | <0.001 |
| Effect of black ethnicity adjusted for… |  |  |
| BMI | 1.20 (1.10, 1.31) | <0.001 |
| Nulliparity | 1.32 (1.18, 1.49) | <0.001 |
| Abnormal foetal heart rate during labour | 0.89 (0.79, 1.01) | 0.065 |
| Late-term birth | 1.35 (1.11, 1.66) | 0.001 |

Table 2: Individually adjusted estimates between ethnicity and MSAF with logistic regression. Nulliparity, abnormal foetal heart rate during labour, and late-term births utilize an interaction coefficient.

Table 3: Final stratified logistic regression model with interaction terms

|  |  |  |  |
| --- | --- | --- | --- |
| Odds of meconium-stained amniotic fluid by **nulliparity** among ethnic categories |  | Adjusted OR (95% c.i.) | P-Value |
| White/Other | Nulliparity (-) | 1.00 REFERENCE |  |
|  | Nulliparity (+) | 1.15 (1.03 1.26) | 0.007 |
| Black | Nulliparity (-) | 1.00 REFERENCE |  |
|  | Nulliparity (+) | 0.96 (0.81 1.14) | 0.630 |
| Main effect of ethnicity in nulliparity negative individuals | White/Other | 1.00 REFERENCE |  |
|  | Black | 0.94 (0.80 1.10) | 0.421 |
| Main effect of ethnicity in nulliparity positive individuals | White/Other | 1.00 REFERENCE |  |
|  | Black | 0.79 (0.65 0.94) | 0.010 |
| Odds of meconium-stained amniotic fluid by **late-term births** among ethnic categories |  |  |  |
| White/Other | Normal-Term | 1.00 REFERENCE |  |
|  | Late-Term | 1.61 (1.45 1.78) | <0.001 |
| Black | Normal-Term | 1.00 REFERENCE |  |
|  | Late-Term | 2.24 (1.83 2.75) | <0.001 |
| Main effect of ethnicity in normal-term births | White/Other | 1.00 REFERENCE |  |
|  | Black | 0.94 (0.80 1.10) | 0.421 |
| Main effect of ethnicity in late-term births | White/Other | 1.00 REFERENCE |  |
|  | Black | 1.31 (1.05 1.64) | 0.018 |
| Odds of meconium-stained amniotic fluid by **abnormal foetal heart rate** (FHR) among ethnic categories |  |  |  |
| White/Other | Normal FHR | 1.00 REFERENCE |  |
|  | Abnormal FHR | 6.10 (5.48 6.76) | <0.001 |
| Black | Normal FHR | 1.00 REFERENCE |  |
|  | Abnormal FHR | 10.67 (8.97 12.69) | <0.001 |
| Main effect of ethnicity in normal foetal heart rate | White/Other | 1.00 REFERENCE |  |
|  | Black | 0.94 (0.80 1.10) | 0.421 |
| Main effect of ethnicity in abnormal foetal heart rate | White/Other | 1.00 REFERENCE |  |
|  | Black | 1.64 (1.35 2.00) | <0.001 |
| Odds of meconium-stained amniotic fluid by **BMI** | Underweight | 0.68 (0.52 0.89) | 0.004 |
|  | Normal | 1.00 REFERENCE |  |
|  | Overweight | 1.20 (1.10 1.33) | <0.001 |
|  | Obese | 1.35 (1.15 1.58) | <0.001 |
|  | Extremely Obese | 1.38 (1.07 1.79) | 0.014 |

Table 3: Stratum-specific estimates for the final logistic regression (cumulatively adjusted) with adjusted ORs and 95% c.i.s. Ethnicity-specific ORs for each variable as well as comparative estimates across ethnic groups are shown.