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ORIGINAL RESEARCH ARTICLE

Birthweight and gestational age in the Faroe Islands: A comparison between birthweight and gestational age in the Faroe Islands and other Nordic countries

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Abstract

Introduction: This study aimed to examine Faroese infants' birthweight and gestational age in 2010–2019 and compare these findings with other Nordic countries. Risk factors for high birthweight among Faroese infants were also investigated in this study.

Material and methods: All singleton liveborn infants registered in the Faroese Birth Registry in 2010–2019 were included in the study ($n = 6121$). A comparison was made with data on birthweight and gestational age from Denmark, Iceland, Norway, and Sweden.

Results: The mean birthweight increased significantly from 3652 g (95% confidence interval [CI]: 3505–3699 g) in 2010 to 3745 g (95% CI: 3700–3790 g) in 2019, a mean increase in birthweight of 93 g (95% CI: 28–158 g) ($p < 0.05$). The birthweight increased 186 g (95% CI: 179–193 g) for each gestational week and 11 g (95% CI: 7–15 g) for each year. Changes in gestational age explained 31% of the change in birthweight. The proportion of infants weighing 4500 g or more increased significantly from 6.1% in 2010 to 9.6% in 2019 ($p < 0.05$). The risk of giving birth to an infant weighing 4000 g or more was consistently associated with previously giving birth (OR 1.98 (95% CI: 1.71–2.30)) and gestational age (OR 1.28 (95% CI: 1.23–1.33) per week increase in gestational age). Infants born in gestational weeks 40 and 42 in 2019 had a higher birthweight z-score than infants born in gestational weeks 40 and 42 in 2010. Compared to other Nordic countries, Faroese infants' mean birthweight was high, the Faroe Islands had a higher number of infants born with a weight of 4000 g or more and a higher proportion of infants born in gestational week 41 or later (31.5%).

Conclusions: Our results showed that the mean birthweight and the proportion of infants with high birthweight significantly increased during 2010–2019 in the Faroe Islands. The mean birthweight, the proportion of infants with high birthweight and

Abbreviations: BW, birthweight; GA, gestational age; FBR, Faroese Birth Registry; CI, confidence intervals; OR, odds ratios.

the gestational age at birth for Faroese infants was higher than all other Nordic countries. The reasons for this require further investigation.

KEYWORDS
development in birthweight, gestational age, high birthweight, macrosomic infants, Nordic countries, the Faroe Islands

1 | INTRODUCTION

The population of the Faroe Islands has been known for its high birthweight (BW) for many years, and it has been discussed why newborns in the Faroe Islands have among the highest BW in the world.[1] A 1980s study showed that Faroese infants had a higher gestational age (GA) and a higher fetal growth rate than Danish peers.[1] Reasons such as different environmental and social determinants in the fishing industry, habits of life and nourishment compared with Denmark have been suggested.[1] More specifically, certain factors in the traditional Faroese lifestyle, such as a high intake of fish, were found compatible with increased BW.[2] Also, the ethnic background has been suggested, as anthropological studies have shown many common characteristics between the Faroese and Icelandic populations, such as high BW.[3,4] An increase in mean BW and the proportion of high BW has previously been detected in many countries across the world,[5–8] and researchers have shown that high BW increases the risk of adverse birth outcomes such as an increased risk of intervention at birth,[9–11] of perineal rupture and postpartum hemorrhage for the mothers as well as the risk of childhood morbidity.[12–15] However, no recent studies have investigated BW and GA in the Faroe Islands. This study aimed to examine Faroese infants' BW and GA in the period 2010–2019 and compare these findings with other Nordic countries. Risk factors for high BW among Faroese infants were also investigated in this study.

Key message

The mean birthweight and the proportion of Faroese infants with high birthweight have significantly increased since 2010 and were higher than in other Nordic countries.

2 | MATERIAL AND METHODS

The Faroe Islands are a group of 18 islands in the North Atlantic Ocean, of which 17 are inhabited. The population counts 54 081 people in total (October 10, 2022).[16] The National Hospital of the Faroe Islands in Tórshavn is the largest of three hospitals, and all hospital births occur here. Data included in this study were derived from the Faroese Birth Registry (FBR), established in 2005. Midwives report the desired information to the chief medical officer, who transfers the information anonymously into a database. The forms the midwives fill out are standardized, easy to complete, and therefore deemed valid. The FBR contains information about all births in the Faroe Islands. Before the FBR was established, the chief medical officer in the Faroe Islands only registered the number of births, place of births and the number of stillbirths.

All singleton liveborn infants with known BW and date of birth registered in the FBR from January 2010 through December 2019 were included in the study (n = 6121). Information on infants' birth date and sex (boy, girl), liveborn or stillborn, BW (grams), GA (completed gestational weeks), mothers' age on the birth date (years), marital status (married, unmarried), smoking status (no, yes) and parity (nulliparous, multiparous) was derived from the FBR.

In this study, we did not include multiple births, stillbirths, or infants with missing data in the FBR. The total number of infants born in 2010–2019 was 6463. Our study included 6121, meaning that 342 infants either had what we categorized as missing data or were stillbirths or multiple births in the period 2010–2019.

Information on BW and GA from Denmark, Iceland, Norway, and Sweden was obtained by contacting Statistics Denmark[17] and The Danish Health Data Authority,[18] The Directorate of Health in Iceland,[19] The Norwegian Institute of Public Health[20] and The National Board of Health and Welfare in Sweden, respectively.[21] We contacted the institutions which respectively provided the requested data by email. Information on average BW of singleton liveborn infants for the years 2010–2019, numbers of singleton liveborn infants with BW categorized into four categories (<4000; 4000–4249; 4250–4499; and ≥4500 g) for the years 2010–2019 and numbers of singleton liveborn infants with GA categorized into three categories (<37; 37–40; 41+ gestational weeks) for the years 2010–2019 was derived for each Nordic country. All singleton infants with known BW and GA (completed gestational weeks) registered in these databases from January 2010 through December 2019 were included in the study. This study included liveborn infants, and it was possible to exclude stillbirths in all databases except The Danish Health Data Authority database. Therefore, stillbirths were included in the proportion of births according to GA for Danish infants.

The data for the Faroese population, the Icelandic population, the Norwegian population, and the Swedish population included all births occurring in the country. Regarding the Danish population, Statistics Denmark includes births of women with residence in Denmark, while The Danish Health Data Authority includes all births occurring in Denmark.

For all populations included in this study, GA and, therefore, also estimated due date was calculated by an ultrasound scan. However, the ultrasound scans are performed at different GAs; The Faroese healthcare system offers a pregnancy ultrasound screening at approximately gestational weeks 18–20. The estimated due date is calculated, and specific congenital anomalies are investigated.[22] The Danish[23] and Norwegian[24] healthcare systems offer all pregnant women a pregnancy ultrasound screening at approximately gestational weeks 12–13 and gestational week 18, where the estimated due date is calculated. The Swedish healthcare system has different guidelines according to the different regions in the country. Generally, it offers an ultrasound screening at approximately gestational week 12 or gestational weeks 18–20, where the estimated delivery date is calculated.[24] The Icelandic healthcare system offers all pregnant women an ultrasound screening at approximately gestational weeks 19–20 and an early fetal screening in gestational weeks 11–14 against payment. The estimated due date is therefore calculated in gestational weeks 11–14 if the pregnant woman accepts this scan, otherwise in gestational weeks 19–20.[25]

2.1 | Statistical analyses

Statistical analyses were performed in R statistics version 3.4.3.[26] We estimated mean BW with 95% confidence intervals (CIs). BW was analyzed both as a continuous variable and categorized into four categories (<4000; 4000–4249; 4250–4499; and ≥4500 g), with high BW defined as BW >4000 g. GA was categorized into three categories (<37; 37–40; 41+ gestational weeks). We made a multiple linear regression model with BW as the dependent variable (continuous), and GA (continuous) and calendar year (categorical) as the independent variables. We included all births from 2010–2019. BW was analyzed as a continuous variable. We calculated the proportions in Table 1 by dividing the number of infants born in the respective group in the respective years by the total number of deliveries in the respective years. We also calculated the proportions for the period 2010–2019 by dividing the number of infants born in the respective group by the total number of deliveries in the period 2010–2019.

We calculated z-scores for the BW of infants born in 2019 and used the BW of infants born in 2010 as reference values. We calculated z-scores by dividing the observed value minus the sample's mean by the sample's standard deviation. Figure 2 shows the mean of the z-scores for gestational weeks 37–42 and 95% CI.

The adjusted associations between the potential risk factors and delivery of a high BW infant are presented as odds ratios (OR) with 95% CIs. The potential risk factors listed in Table 2 were all considered in a multivariable logistic regression model as a number of dummy variables equal to the number of categories minus one, and the mutually adjusted odds ratios are presented. The weight reference was 2500–3999 g.

The differences between the two categorical variables were calculated using the chi-square test. The differences between two independent samples with equal variances were calculated using a *t*-test as the data was normally distributed. We considered a *p*-value <0.05 as statistically significant.

2.2 | Ethics statement

The study was approved by the National Hospital of the Faroe Islands on October 21, 2020. Approval number 125–21/01725.

3 | RESULTS

3.1 | Development in BW and high BW over time

The mean BW for all infants increased significantly from 3652 g (95% CI: 3505–3699 g) in 2010 to 3745 g (95% CI: 3700–3790 g) in 2019, a mean increase in BW of 93 g (95% CI: 28–158 g) ($p<0.05$) (Figure 1 and Table 1). Our results showed that for each gestational week, the BW increased 186 g (95% CI: 179–193 g), and for each year, the BW increased 11 g (95% CI: 7–15 g). Changes in GA explained 31% of the change in BW.

The proportion of women who gave birth to their first child decreased from 36.2% in 2010 to 34.3% in 2019. Additionally, the cesarean section rate remained essentially unchanged, decreasing from 18.1% in 2010 to 17.2% in 2019.

The overall frequency of infants with BW higher than 4000 g for 2010–2019 was 29.6% ($n = 1814$). The proportion of infants with high BW rose during the study period. The proportion of infants with a BW of 4000 g or more increased from 26.0% in 2010 to 30.8% in 2019 ($p = 0.07$), while the proportion of infants weighing 4500 g or more increased significantly from 6.1% in 2010 to 9.6% in 2019 ($p<0.05$). The proportion of births delivered after 40 completed weeks of gestation increased from 35.0% in 2010 to 40.1% in 2019 ($p = 0.07$).

Our study showed that infants born in gestational week 40 in 2019 had a BW *z*-score 0.17 units (95% CI: 0.03–0.31) higher than infants born in gestational week 40 in 2010 (Figure 2). Additionally, our study showed that infants born in gestational week 42 in 2019 had a BW *z*-score 0.36 units (95% CI: 0.06–0.65) higher than infants born in gestational week 42 in 2010 (Figure 2).

Our study showed that in the period 2010–2019, Faroese infants' mean BW was higher compared to other Nordic countries (Figure 1). Our study also showed that the proportion of infants in the Faroe Islands with high BW was higher than in other Nordic countries (Figure 3). This applied for the three categories 4000–4249 g, 4250–4499 g and ≥4500 g (Figure 3). Additionally, our study showed that the Faroe Islands has a lower proportion of infants born between gestational weeks 37 and 40 and a higher proportion of infants born in gestational week 41 or later in the period 2010–2019 compared to other Nordic countries (Figure 4). The difference in the distribution

TABLE 1 Comparing the differences in average birthweight, the proportion of high birthweight and the proportion of births according to gestational age between different Nordic countries.

	The Faroe Islands	Denmark[a]	Iceland[b]	Norway[c]	Sweden[d]
Average birthweight (g)					
2010	3652	3512	3662	3525	3543
2011	3641	3503	3646	3525	3539
2012	3674	3500	3635	3521	3541
2013	3715	3500	3628	3526	3541
2014	3692	3495	3657	3526	3534
2015	3720	3499	3643	3527	3533
2016	3725	3507	3633	3521	3531
2017	3710	3517	3632	3527	3535
2018	3784	3517	3623	3527	3528
2019	3745	-	3628	3538	3523
The proportion of high birthweight (%)					
2010–2014					
4000–4249 g	14.0	9.5	12.8	9.9	10.0
4250–4499 g	8.6	4.6	6.7	4.9	5.2
≥4500 g	5.7	2.8	4.8	3.1	3.6
2015–2019					
4000–4249 g	14.2	9.7[e]	12.4	10.0	8.2
4250–4499 g	8.9	4.7[e]	6.7	5.0	4.2
≥4500 g	7.8	2.9[e]	4.5	3.0	2.8
2010–2019					
4000–4249 g	14.1	9.6[f]	12.6	9.9	9.9
4250–4499 g	8.7	4.7[f]	6.7	5.0	5.1
≥4500 g	6.8	2.9[f]	4.6	3.1	3.5
The proportion of births according to gestational age (%)					
2010–2014					
<37	3.9	4.2[g]	4.1	4.8	4.7
37–40	63.5	69.7[g]	71.5	68.8	70.4
41+	32.6	26.1[g]	24.4	25.9	25.0
2015–2019					
<37	3.3	4.2[e,g]	4.8	4.7	3.8
37–40	66.3	69.3[e,g]	73.2	70.3	58.5
41+	30.5	26.4[e,g]	22.0	24.9	21.5
2010–2019					
<37	3.6	4.2[f,g]	4.4	4.7	4.6
37–40	64.9	69.5[f,g]	72.3	69.8	70.1
41+	31.5	26.2[f,g]	23.2	25.5	25.3

Abbreviation: g, grams.

[a]The statistics are provided by Statistics Denmark and The Danish Health Data Authority. Available from: www.dst.dk and www.sundhedsdatastyrelsen.dk.

[b]The statistics are provided by The Directorate of Health. Available from: www.landlaeknir.is.

[c]The statistics are provided by The National Board of Health and Welfare in Sweden. Available from: www.socialstyrelsen.se.

[d]The statistics are provided by The Norwegian Institute of Public Health. Available from: www.fhi.no.

[e]Calculated for the period 2015–2018.

[f]Calculated for the period 2010–2018.

[g]Includes stillbirths.

TABLE 2 Multivariate logistical analysis of risk factors for high birthweight in the Faroe Islands, 2010–2019. Weight reference 2500–3999 g.

	Weight reference 2500–3999 g	All weights ≥4000 g		4000–4249 g		4250–4499 g		≥4500 g	
	n	*n*	OR (95% CI)	*n*	OR (95% CI)	*n*	OR (95% CI)	*n*	OR (95% CI)
Maternal age[a]	4181	1814	1.00 (0.99 to 1.01)	864	1.00 (0.98 to 1.01)	534	0.99 (0.97 to 1.01)	416	1.01 (0.98 to 1.03)
Marital status									
Unmarried	2421	972	1.00	466	1.00	292	1.00	214	1.00
Married	1760	842	1.03 (0.91 to 1.16)	398	1.08 (0.92 to 1.27)	242	1.03 (0.84 to 1.26)	202	1.11 (0.89 to 1.39)
Gender									
Male	1988	1057	1.00	481	1.00	320	1.00	256	1.00
Female	2193	757	0.69 (0.62 to 0.77)	383	0.74 (0.64 to 0.86)	214	0.63 (0.52 to 0.77)	160	0.61 (0.49 to 0.75)
Smoking									
No	3608	1661	1.00	778	1.00	501	1.00	382	1.00
Yes	573	153	0.68 (0.57 to 0.82)	86	0.71 (0.55 to 0.91)	33	0.43 (0.29 to 0.61)	34	0.61 (0.41 to 0.89)
Parity									
First birth	1621	486	1.00	248	1.00	149	1.00	89	1.00
Previously given birth	2560	1328	1.98 (1.71 to 2.30)	616	1.74 (1.45 to 2.10)	385	2.00 (1.58 to 2.53)	327	2.55 (1.93 to 3.39)
Gestational age[b]	4181	1814	1.28 (1.23 to 1.33)	864	1.64 (1.54 to 1.75)	534	1.86 (1.71 to 2.02)	416	2.05 (1.87 to 2.26)
Year[c]	4181	1814	1.02 (1.00 to 1.04)	864	1.01 (0.98 to 1.04)	534	1.03 (0.99 to 1.06)	416	1.07 (1.03 to 1.11)

Abbreviations: CI, confidence interval; g, grams.

[a]Odds ratio for a one-year change in age.

[b]Odds ratio for a 1 week change in gestational age.

[c]Odds ratio for a one-year change in calendar time.

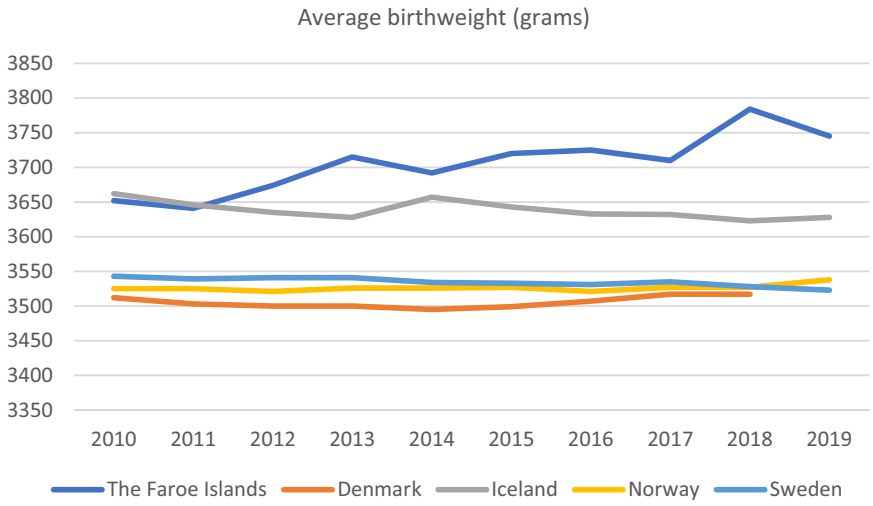

FIGURE 1 Average birthweight in different Nordic countries in the period 2010–2019.

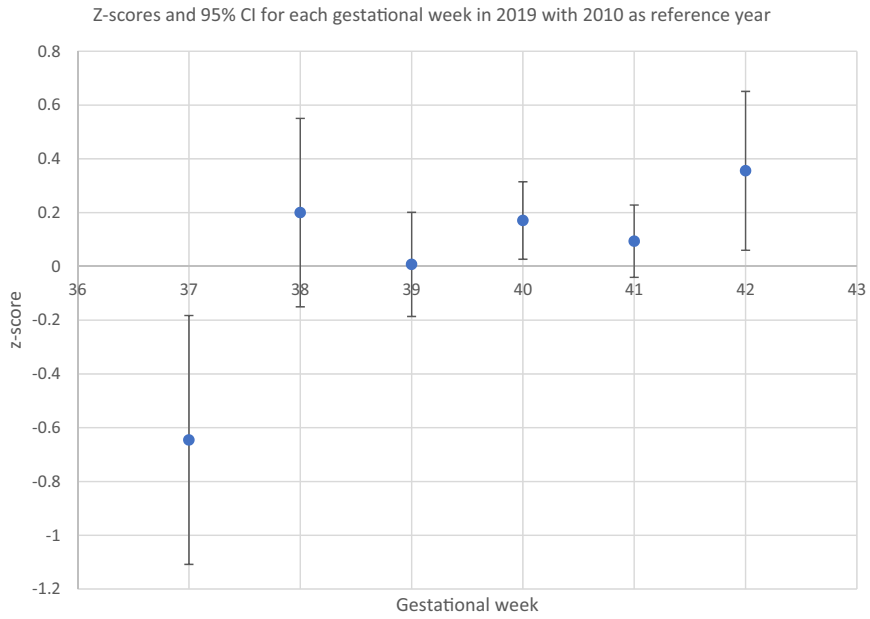

FIGURE 2 Z-scores and 95% confidence interval (CI) for each gestational week in 2019 with 2010 as reference year.

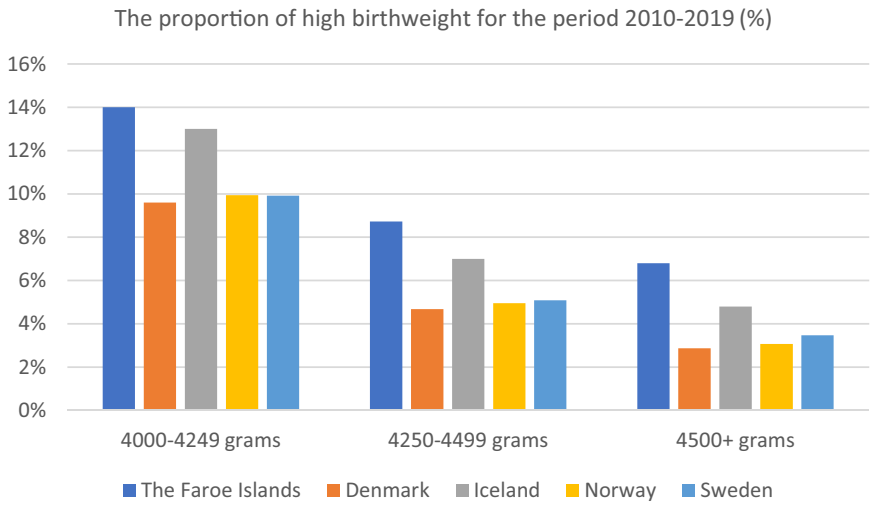

FIGURE 3 The proportion of high birthweight in different Nordic countries throughout the period 2010–2019.

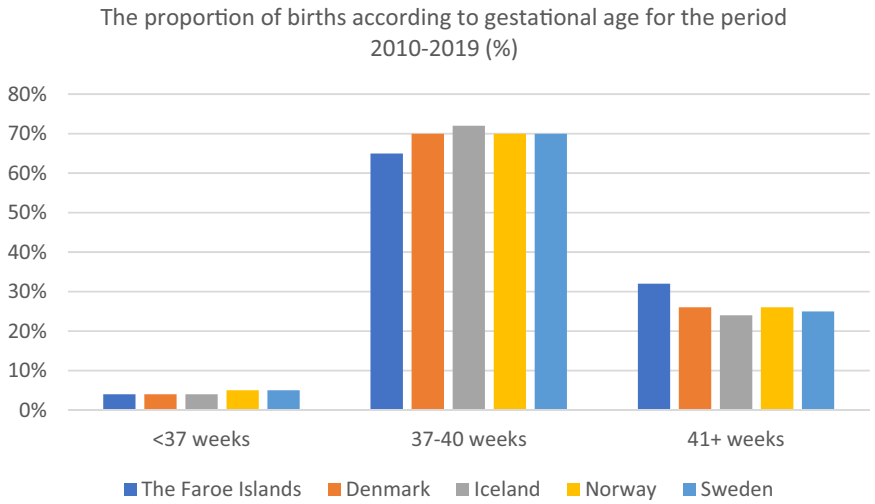

FIGURE 4 The proportion of births according to gestational age throughout the period 2010–2019.

of GA between the Faroe Islands and the other Nordic countries was not statistically significant.

3.2 | Risk factors for high BW

Table 2 shows the risk factors for high BW in the Faroe Islands for 2010–2019. Infant female gender (OR 0.69 [95% CI: 0.62–0.77]) and maternal smoking (OR 0.68 [95% CI: 0.57–0.82]) were associated with a reduced risk of giving birth to an infant weighing 4000 g or more (Table 2). Multiparous women (OR 1.98 [1.71–2.30]) and high GA (OR 1.28 [95% CI: 1.23–1.33]) were associated with an increased risk of giving birth to an infant weighing 4000 g or more (Table 2). Multiparous women had twice the risk of giving birth to an infant weighing 4250–4499 g (OR 2.00 [95% CI: 1.58–2.53]) and two and a half times higher risk of giving birth to an infant weighing 4500 g or more than nulliparous women (OR 2.55 [95% CI: 1.93–3.39]) (Table 2). Additionally, for every one-week increase in GA, infants were twice as likely to weigh 4500 g or more (Table 2).

4 | DISCUSSION

In this study, we retrospectively investigated 6121 singleton live-born Faroese infants from 2010–2019. We found that the mean BW increased significantly with 93 g from 2010 to 2019 and that the BW increased by 186 g for each gestational week and 11 g for each year. We found that infants born in gestational weeks 40 and 42 in 2019 had a higher BW z-score than infants born in gestational weeks 40 and 42 in 2010. We also found that the proportion of infants weighing 4500 g or more increased significantly from 6.1% in 2010 to 9.6% in 2019. An increase in mean BW and the proportion of high BW has previously been detected in many countries worldwide.[5–8] In recent years, however, our data suggest that this increase has not been observed in other Nordic countries. A recent study found a distinct rise and then a decline to previous levels in mean birthweights in Norway, indicating no apparent explanations for this plateau.[27] An increase in mean BW and the proportion of high BW can indicate a healthy society with a high standard of antenatal care and a high standard of living. It can be an indicator of a reduced number of infants with low BW, which is mainly positive, but it can also be an indicator of an increased number of infants with high BW, the benefits of which are more unclear. High BW is associated with an increased risk of intervention at birth, such as cesarean section,[9,10] more frequent use of episiotomy and instrumental delivery.[11] Additionally, high BW is associated with increased risks of perineal rupture and postpartum hemorrhage for the mothers, neurological sequelae and perinatal deaths for the infants.[9,12,28] High BW is also associated with an increased risk of certain childhood cancers and with long-term health risks such as obesity, type 2 diabetes and an increased risk of breast cancer and prostate cancer in adulthood.[29–34] However, the risk of, for example, cardiovascular disease has been shown to be lower. Our study did not investigate if Faroese infants and their mothers have an increased risk of adverse birth outcomes or increased risks of childhood and adult morbidity.

Our results showed that female child gender and smoking were associated with a reduced risk of giving birth to an infant weighing 4000 g or more. Our results also showed that multiparous women and high GA were associated with an increased risk of giving birth to an infant weighing 4000 g or more. Similar trends are seen in other studies.[8,35]

Additionally, our study showed that Faroese infants' mean BW was higher than other Nordic countries (Figure 1) and that the Faroe Islands have a higher number of infants born with a weight of 4000 g or more than other Nordic countries (Figure 3). A 1980s study found that Faroese infants had a higher fetal growth rate than Danish peers.[1] Different eating habits in terms of a higher intake of fish and a different ethnic background compared to other countries have been suggested to be reasons for this.[2–4] The fishing industry is an integral part of the Faroese society, and fish is a significant part of the Faroese cuisine. However, the Faroese eating habits have been shown to have changed during the last century as society has

become more modernized.[36] It is, therefore, doubtful if the Faroese women had a higher intake of fish in the period 2010–2019 compared to other Nordic countries, and therefore also doubtful if this could be a reason for the Faroese infants' high and increasing BW in the period 2010–2019.[37]

Our study has not investigated causes for the increasing mean BW and the increasing proportion of infants with high BW and why these factors are higher in the Faroe Islands compared to other Nordic countries in 2010–2019. A hypothesis could be that the high number of hereditary genetic conditions in the Faroe Islands could be a reason for the Faroese infants' high BW compared to other Nordic countries. The population in the Faroe Islands has a high degree of genetic heredity because the Faroese people constitute a geographically isolated population.[38,39] Figures 1 and 3 show that Icelandic infants' BW is just below the Faroese infants', which strengthens this hypothesis because Icelandic people constitute a geographically isolated population, too.[40,41]

Possible explanations for the increasing mean BW and the proportion of high BW are an increase in maternal prepregnant BMI and in pregnancy weight gain and a decrease in the proportion of smoking women, which studies have shown to be strongly positively associated with BW.[35,42,43] Information on maternal weight and pregnancy weight gain was not available in our data. However, a hypothesis could be that Faroese women have a higher prepregnant BMI and a higher pregnancy weight gain compared to other Nordic countries and that this also is the reason for the increase of Faroese infants' mean BW and in the proportion of high BW in the period 2010–2019.

Temporal shifts in mean BW and the proportion of infants with high BW have been observed in several populations, and no apparent explanations for these shifts have been detected.[27,44] A hypothesis could, therefore, also be that the increase of Faroese infants' mean BW and the proportion of high BW in the period 2010–2019 forms part of a more extended period, where the BW is reaching a plateau and declining to previous levels.

Our study showed that the Faroe Islands has a lower proportion of infants born between gestational weeks 37 and 40 and a higher proportion of infants born in gestational week 41 or later in the period 2010–2019 compared to all other Nordic countries (Figure 4). Faroese women whose pregnancy is longer than the estimated delivery date and who have an uncomplicated pregnancy are offered labor induction at 42 gestational weeks and 0 days. This does not comply with guidelines in other Nordic countries, which usually offer labor induction no later than 41 gestational weeks and 5 days.[45] The fact that uncomplicated pregnancies are offered labor induction earlier in the other Nordic countries than the Faroe Islands makes it possible that complicated pregnancies are also offered earlier induction in the other Nordic countries compared to the Faroe Islands. The higher proportion of infants born in gestational week 41 or later and the later offer of induction could also explain a part of the high numbers of Faroese infants with high BW, as GA is a vital contributor to birthweight. Our study showed that changes in GA explained 31% of the change in BW. Unfortunately, no information on labor induction was available from the National Hospital of the Faroe Islands.

The differences in GA, mean BW and the proportion of high BW infants between the Nordic countries could hypothetically also be explained by other external factors, such as the possible differences in the proportion of immigrant women. This could be assessed in future studies.

Our study has some limitations. First, the populations from the Faroe Islands and the other Nordic countries are not entirely comparable. The data for the Faroese, Icelandic, Norwegian, and Swedish populations included all births occurring in the country. Regarding the Danish population, Statistics Denmark includes births of women with residence in Denmark, while The Danish Health Data Authority includes all births occurring in Denmark. Second, regarding Danish infants, we could not acquire the average BW, the proportion of high BW and the proportion of births according to GA for 2019. Also, we could not exclude stillbirths in the proportion of births according to GA for the Danish infants, which is why Table 1 and Figure 4 include stillbirths. This means that these results are only partially compatible with the remaining results. Third, the different countries calculated the estimated due date by ultrasound scan, which is good for comparability. However, some countries estimated this date at a different time in the pregnancy, which may impact GA estimation. This means that that the GA may be only partially compatible between the countries.

5 | CONCLUSION

Our study presents Faroese infants' BW and GA in the period 2010–2019 and compares these findings with other Nordic countries. Our study also presents risk factors for high BW among Faroese infants. Our results showed that the mean BW and the proportion of infants with high BW significantly increased from 2010–2019 in the Faroe Islands. The mean BW, the proportion of infants with high BW and the GA for Faroese infants is higher than in other Nordic countries in 2010–2019. The reasons for this require further investigation.

AUTHOR CONTRIBUTIONS

SHO and USK designed the study. SHO and HH analyzed data or performed statistical analysis. SHO drafted the manuscript. SHO, DR and USK critically revised the manuscript for important intellectual content. SHO is the guarantor of this work and, as such, has had full access to all the data in the study and takes responsibility for the integrity of the data and the accuracy of the data analysis. All authors read and approved the final manuscript.

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CONFLICT OF INTEREST STATEMENT

The authors declare no conflict of interest.

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