宮崎大学学術情報リポジトリ
University of Miyazaki Academic Repository

Comparison of serum concentrations of pregnancy-associated glycoproteins and estrone sulphate during pregnancy in eutocia and dystocia beef cattle

メタデータ	言語: English
	出版者: Elsevier BV
	公開日: 2024-06-14
	キーワード (Ja):
	キーワード (En): Cattle, Dystocia, Estrone sulphate, Pregnancy-associated glycoproteins
	作成者: Maeda, T., 北原, 豪, 大澤, 健司
	メールアドレス:
	所属:
URL	http://hdl.handle.net/10458/0002000683

This work is licensed under a Creative Commons Attribution 4.0 International License.

The Veterinary Journal 305 (2024) 106147

Contents lists available at ScienceDirect

The Veterinary Journal

journal homepage: www.elsevier.com/locate/tvjl

Comparison of serum concentrations of pregnancy-associated glycoproteins and estrone sulphate during pregnancy in eutocia and dystocia beef cattle

T. Maeda [a], G. Kitahara [b], T. Osawa [b,*]

[a] Miyakonojyo Livestock Clinic, Miyazaki Agricultural Mutual Aid Association, Miyakonojyo, Miyazaki, Japan

[b] Laboratory of Theriogenology, Department of Veterinary Sciences, Faculty of Agriculture, University of Miyazaki, Japan

ARTICLE INFO

Keywords:
Cattle
Dystocia
Estrone sulphate
Pregnancy-associated glycoproteins

ABSTRACT

Preventing dystocia can stabilise beef cattle management. This study aimed to investigate the relationship between serum pregnancy-associated glycoproteins (PAGs) S-N values and estrone sulphate (E_1S) concentrations during pregnancy and the calf birth weight in beef cattle and to evaluate their usefulness as new predictive parameters for dystocia due to foetal overgrowth. Thirty-eight pregnant Japanese Black cattle were used. Blood samples were collected at 40, 70, 100, 150, 200, 250, 280, and 285 days after artificial insemination (AI), and birth weight of the offspring was measured. Serum PAGs S-N values and E_1S concentrations were measured, and the area under the curve (AUC) and the ratio of change based on 70 days after AI were calculated, followed by calculation of the correlation coefficient with the birth weight of the offspring and comparison between the eutocia ($n = 32$) and dystocia ($n = 6$) groups. The birth weight of the offspring was moderately positively correlated with the AUC of serum PAGs S-N values and E_1S concentrations in the second ($r = 0.425$, $P < 0.01$) and third ($r = 0.595$, $P < 0.01$) trimesters, respectively. The ratio of change in serum E_1S concentrations between 70 and 280 days after AI was greater ($P < 0.05$) in the dystocia group (1276.6 ± 229.1 %) than in the eutocia group (852.6 ± 69.6 %). These results suggest that blood PAGs S-N values at mid-pregnancy (100–199 days after AI) and the ratio of changes in blood E_1S concentrations between 70 and 280 days after AI may be new parameters for predicting dystocia.

1. Introduction

Bovine dystocia not only causes stillbirths and neonatal death but also induces birth canal damage in the dam, which negatively affects subsequent reproductive performance (Bellows et al., 2002; Sasaki et al., 2014; Mekonnen and Moges, 2016). Successful pregnancies and calving are among the most important factors in beef cattle management.

Dystocia in beef cattle is the cause of 21.3 % of stillbirths, with dystocia rates ranging from 3.8 % to 17.8 % (Uematsu et al., 2013; Bragg et al., 2021). Dystocia is caused by an interrelationship between foetal factors, such as oversized, displaced, multiple, and malformed foetuses, and maternal factors, such as an abnormal birth canal and labour (Weldeyohanes and Fesseha, 2020), of which excessive foetal size is the most common, and calf birth weight is the most important predictor of dystocia (Johanson and Berger, 2003; Maeda et al., 2022).

The placenta is an organ that transports respiratory gases, nutrients, and waste products between dams and the foetus, and abnormal placental function can lead to intrauterine growth retardation of the foetus and stillbirths (Ogata et al., 1995; Reynolds et al., 2010). Placental weight and cotyledon surface area are positively correlated with birth weight (Echternkamp, 1993; Sullivan et al., 2009; Dunlap et al., 2015; Redifer et al., 2021; Miguel-Pacheco et al. 2017), and hormones secreted by the placenta may be possible parameters for predicting birth weight and the occurrence of dystocia.

Bovine placental trophoblast binuclear cells are maintained at 15–20 % in chorioallantoic cells during pregnancy (Wooding, 2022) and play a central role in placental hormone production. Pregnancy-associated glycoproteins (PAGs) are composed of a group of closely related proteins, each of which has been identified as having approximately 20 different molecular species, each with diverse expression patterns (Green et al., 2000). The dynamics of blood PAGs concentrations from breeding to calving have been reported in dairy and beef cattle (Mercadante et al., 2013; Shahin et al. 2014; Fontes et al. 2019). Estrone sulphate (E_1S), a steroid hormone synthesised in the

* Correspondence to: Laboratory of Theriogenology, Department of Veterinary Sciences, Faculty of Agriculture, University of Miyazaki Gakuenkibanadai Nishi 1-1, Miyazaki, 889-2192, Japan.

E-mail address: osawa@cc.miyazaki-u.ac.jp (T. Osawa).

https://doi.org/10.1016/j.tvjl.2024.106147
Received 31 January 2024; Received in revised form 5 April 2024; Accepted 23 May 2024
Available online 27 May 2024
1090-0233/© 2024 The Authors. Published by Elsevier Ltd. This is an open access article under the CC BY license (http://creativecommons.org/licenses/by/4.0/).

foetal and cotyledonary portions of the placenta, is also considered a practical indicator of placental function and is associated with the placental weight, cotyledon weight, and cotyledonary surface area, as well as blood PAGs concentrations (Takahashi et al. 1997; Patel et al. 1999; Hirako et al. 2002, Isobe et al., 2003; Sullivan et al., 2009). Finding blood parameters to monitor the pregnancy process would contribute to reducing stillbirth rates. However, there have been no reports on the relationship between blood PAGs and E_1S concentrations or dystocia due to excessive foetal size.

The objective of this study was to clarify the relationship between serum PAGs S-N values and E_1S concentrations during pregnancy and the birth weight of offspring that delivered normally and experienced dystocia, in order to investigate a new method of predicting dystocia due to excessive foetal size using blood hormonal levels in beef cattle.

2. Materials and methods

This study was approved by the Miyazaki University Animal Experiment Committee (Approval No. 2021–037).

2.1. Animals

In this study, we tested 40 Japanese Black cattle (4.0 ± 2.7 parity, mean ± standard deviation) bred on a commercial farm in Miyazaki Prefecture, Japan. The cattle were artificially inseminated with frozen semen from a Japanese Black bull for 28–168 days after the previous calving, and conception was confirmed by ultrasonography at 40 days after artificial insemination (AI). The cattle were housed at approximately six cows per plot from 7 days after the last calving until 255 days in pregnancy and fed a total mixed ration (TMR) (74.3 % dry matter [DM], 62.1 % total digestible nutrients [TDN], and 12.2 % crude protein [CP]) twice a day (9 kg/day). Thirty days before calving (255 days gestation), they were housed individually in 4–16 m^2 calving pens and fed 5 kg of TMR plus 2 kg of breeding formula (87.1 % DM, 78.0 % TDN, 17.6 % CP) and 4 kg of oats hay until the day of calving. Two farm employees stayed on the farm during the night to monitor calving. Of the 40 cattle, ten cows were assisted in calving, all because the foetus was oversized relative to the maternal pelvis. Of these ten cows, four were assisted lightly by one farm employee, and six were assisted heavily by two to three farm employees using calving assistance equipment. In this study, eutocia was clinically defined as the ability of the dam to deliver a foetus without substantial obstetrical assistance (Simões and Stilwell, 2021), and dystocia was defined as calving assisted by two or more farm employees using calving assistance equipment. There were no dystocia due to abnormal deliveries, including foetal malformations or multiple births. Two calved twins, one of which had a stillbirth, and both received no calving assistance. The remaining 38 cows calved their singletons via anterior presentation. The gender breakdown of the calves was 21 females (34.2 ± 5.4 kg) and 17 males (37.6 ± 3.6 kg).

2.2. Blood sample collection and storage

Blood was collected from the jugular vein eight times at 40, 70, 100, 150, 200, 250, 280, and 285 days after AI using a blood collection holder with a 21 G blood collection needle (Venoject® II blood collection needle S, Terumo Corporation, Tokyo) set into a 10 mL plain vacuum blood collection tube (Venoject® II, Terumo Corporation, Tokyo, Japan). After blood collection, the tubes were immediately incubated in a water bath at 37 °C for 15 min to precipitate fibrin, and then centrifuged (Spectrafuge 6C, Labnet International, USA) at 855.3 × *g* for 15 min. After centrifugation, the tubes were placed in a cooler box at 15 °C and brought back to the laboratory within 40 min. Two millilitre of obtained serum was dispensed into 2 mL tubes (Eppendorf Safe-Lock Tubes 2.0 mL, Eppendorf Corporation, Tokyo) and stored at - 21 °C until further analysis.

2.3. Measurement of PAGs

Serum PAGs S-N values were measured by sending the serum that had been frozen and stored for 8 months after collection to IDEXX Laboratories (Koganei, Tokyo, Japan) using the Alertys Ruminant Pregnancy Test Kit (RPT), according to previous reports (Ricci et al. 2015; Roberts et al. 2017; Northrop et al. 2019). RPT is an enzyme-linked immunoassay that uses plates coated with anti-PAG antibodies (PAG-4, PAG-6, PAG-9, PAG-16, PAG-18, and PAG-19) to quantify PAGs S-N values. The measurements were performed according to the manufacturer's instructions. The absorbance of the controls and each serum sample was measured at 420 and 620 nm, using Multiskan FC (Thermo Fisher Scientific). The absorbance of the negative and positive controls, which were set up in two wells each, was the average absorbance value of the two wells. Serum PAGs S-N values was calculated as the S-N value by subtracting the average absorbance of the negative control from the absorbance of each sample. The sensitivity of the assay was 0.030 and the within-assay and between-assay coefficients of variation ranged from 1.2 % to 4.2 %.

2.4. Measurement of E_1S

Serum E_1S concentrations were measured using Estrone-3-Sulphate (E_1S) ELISA Kits (ARBOR ASSAYS, Ann Arbor, Michigan, USA). Serum E_1S concentrations were determined by operating according to the manufacturer's instructions and using a microplate reader (Multiskan Go, Thermo Fisher Scientific, USA) to read the optical density at 450 nm and by calculating the E_1S concentrations for each sample. The assay sensitivity was 29.7 pg/mL, and the intra- and inter-assay coefficient of variation ranged from 2.3 % to 9.2 % and 3–8.9 %, respectively.

2.5. Measurement of birth weight in offspring

The birth weights of the 38 offspring were measured within 12 h of birth using an analogue scale for humans (Analogue Health Mater HA-851; Tanita Corporation, Tokyo, Japan).

2.6. Statistical analysis

Data from 38 of the 40 cows were used, excluding two twins and eight cows that calved between 280 and 285 days after AI, resulting in 30 cows at 285 days. Each measurement was checked for normality and the correlation coefficient with cow parity was calculated using Spearman's rank correlation coefficient and compared between female and male calves using Student's t-test or Mann-Whitney U-test. The mean serum PAGs S-N values and E_1S concentrations at each blood collection time point were checked for normality. Analysis of variance with repeated measures was applied, and comparisons were made using multiple comparison tests.

The area under the curve (AUC) of serum PAGs S-N values and E_1S concentrations during each blood collection interval was calculated by linear trapezoidal method using the following formula (Schwartz and Pateman, 2021), and after confirming normality, the correlation coefficient with the birth weight of calves was respectively calculated by Pearson's correlation coefficient or Spearman's rank phase relation number.

AUC = 0.5 × (PAGs S-N values or E_1S concentrations at a blood collection point + PAGs S-N values or E_1S concentrations at the next blood collection point) × (days between blood collection points)

In Japanese Black cattle, the average birth weight of offspring delivered without assistance has been reported to be in the range of 34.4–36.4 kg (Sakatani et al., 2018; Maeda et al., 2022), and the dystocia group in this study weighed > 37 kg. Therefore, the 38 cows were divided into groups of < 37.0 kg (< 37 kg group; n = 18) and ≥ 37.0 kg (≥ 37 kg group; n = 20), based on 37.0 kg, and serum PAGs and E_1S concentrations were compared between the two groups. Mean serum PAGs and E_1S concentrations for each post insemination day between the two groups were compared using Student's t-test after checking for normality and equal variance.

Of the 38 cattle, 32 were classified into the eutocia group (28 cattle that calved normally and four cattle that were assisted lightly by one farm employee) and six cattle that were assisted by two to three farm employees using calving assistance equipment were classified into the dystocia group. The gestational period was divided into three semesters: first trimester (40–99 days), second trimester (100–199 days), and third trimester (200–280 days) after AI, respectively. The AUC of serum PAGs and E_1S concentrations were calculated for each period and compared between the eutocia and dystocia groups. The AUC of mean serum PAGs and E_1S concentrations for each post-insemination day between the two groups were compared using the Student's t-test after confirming normality and equal variance.

In the profiles of mean serum PAGs and E_1S concentrations, the ratio of change was calculated based on 70 days after AI [(each concentration - the concentration at 70 days after AI) / the concentration at 70 days after AI × 100], when both hormone concentrations were at their lowest point, and then compared between the eutocia and dystocia groups using the Student's t-test after checking for normality and equal variance.

Statistical analysis was performed using EZR statistical software (Saitama Medical Center, Jichi Medical University) (Kanda, 2013). Data are presented as mean ± standard deviation or mean ± standard error, with a significance level of $P < 0.05$.

3. Results

The mean serum PAGs S-N values of the 38 pregnant cattle temporarily decreased significantly from 40 to 70 days, recovered at 100 days, and increased significantly from 150 to 285 days after AI (Fig. 1). Mean serum E_1S concentrations in the 38 cattle remained low from 40 to 100 days, and then gradually increased significantly from 200 to 280 days after AI (Fig. 1).

Correlation coefficients between the AUC of serum PAGs and E_1S concentrations in the first, second, and third trimesters of pregnancy and the calf birth weight were calculated. The birth weight of the offspring was moderately positively correlated with the AUC of serum PAGs S-N values in the second trimester ($r = 0.425$, $P < 0.01$) and with the AUC of serum E_1S concentrations in the third trimester ($r = 0.595$, $P < 0.01$) (Fig. 2).

Moderate positive correlations were found between the AUC of serum PAGs S-N values from 100 to 250 days and the AUC of serum E_1S concentrations from 150 to 285 days after AI and the birth weight of the offspring (Table 1).

The mean serum PAGs and E_1S concentrations were compared between the ≥ 37 kg and < 37 kg group. The ≥ 37 kg group had higher mean serum PAGs S-N values at 150 and 200 days after AI ($P < 0.05$), and higher mean serum E_1S concentrations at 280 and 285 days after AI ($P < 0.01$) than the < 37 kg group (Fig. 3). Comparison of the AUC of the mean serum PAGs and E_1S concentrations in the first, second, and third trimesters of pregnancy showed no difference between the two groups (Fig. 4).

The ratio of change in serum E_1S concentrations at 280 days to 70 days after AI was greater in the dystocia group (n = 6; 1276.6 ± 229.1 % [mean ± standard error]) compared to the eutocia group (n = 32; 852.6 ± 69.6 %) ($P < 0.05$, Fig. 5).

No association was found between cow parity and calf sex and measurements of PAGs and E_1S.

4. Discussion

This study was conducted to measure blood PAGs S-N values and E_1S concentrations during pregnancy and after eutocia and dystocia delivery in beef cattle, and to clarify the relationship between the birth weight of offspring and their dynamics. The birth weight was associated with serum PAGs S-N values in the second trimester of pregnancy, suggesting that serum PAGs S-N values may be a parameter to identify cows at risk of dystocia earlier than the serum E_1S concentrations. The profiles of mean serum PAGs S-N values in Japanese Black cattle showed a temporary decrease from 40 to 70 days, followed by a gradual increase until 285 days after AI. The profile of blood PAGs S-N values in Holstein breeds using the same assay kit as that used in this study was reported to increase from 25 to 32 days with an S-N value of 2.5, with the lowest point (S-N value 1.0) from 53 to 60 days, followed by an S-N value of 2.0

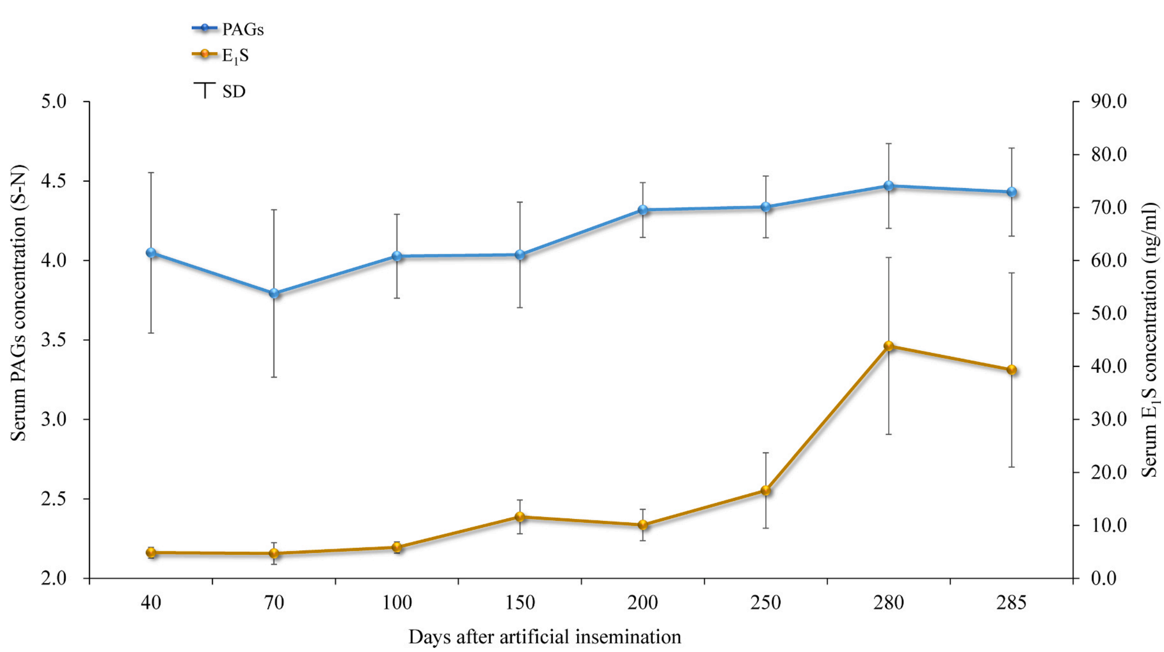

Fig. 1. Profiles of pregnancy-associated serum glycoproteins (PAGs) S-N values and estrone sulphate (E_1S) concentrations from 40 to 285 days of pregnancy in Japanese Black cows. Data are presented for 38 cows from 40 to 280 days after artificial insemination (AI) and for 30 cows from 280 to 285 days after AI because eight cows calved somewhere between 281 and 285 days of pregnancy. Data are presented as mean ± standard deviation (SD).

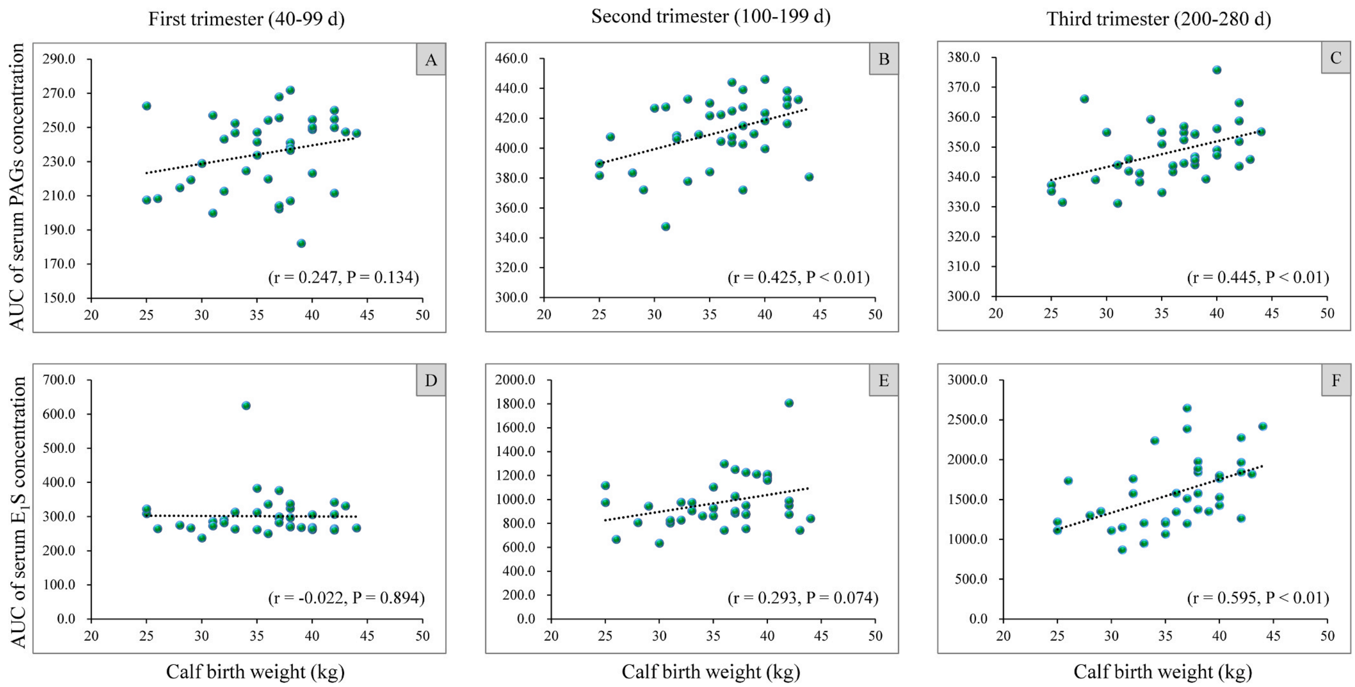

Fig. 2. Correlation coefficients (r) between area under the curve (AUC) of serum pregnancy-associated glycoproteins (PAGs) S-N values (A, B, C) and estrone sulphate (E_1S; D, E, F) concentrations and calf birth weight. (A), (D): First trimester (40–99 days of pregnancy) (B), (E): Second trimester (100–199 days of pregnancy) (C), (F): Third trimester (200–280 days of pregnancy).

Table 1
Correlation coefficient (r) between area under the curve of serum pregnancy-associated glycoproteins S-N values and estrone sulphate concentrations at each period and the birth weight of the calves.

	PAGs		E_1S	
Days after AI	r	P - value	r	P - value
40–70 (n = 38)	0.158	0.343	-0.074	0.661
70–100 (n = 38)	0.274	0.096	0.073	0.664
100–150 (n = 38)	0.405	0.012	0.264	0.109
150–200 (n = 38)	0.407	0.011	0.353	0.030
200–250 (n = 38)	0.411	0.012	0.423	0.008
250–280 (n = 38)	0.314	0.055	0.453	0.004
280–285 (n = 30)[a]	-0.205	0.277	0.630	0.000

PAGs, pregnancy-associated glycoproteins; E_1S, estrone sulphate.
[a] Data from 38 cows were used from 40 to 280 days after artificial insemination (AI), and eight cows were calved between 280 and 285 days after artificial insemination (AI), resulting in 30 cows at 285th day.

from 74 to 102 days after timed AI (TAI) (Ricci et al., 2015). Therefore, we expected that blood PAGs S-N values in Japanese Black cattle would show a similar transition, although there are differences in concentrations between Holstein and Japanese Black cattle. The profiles of blood PAGs S-N values in beef cattle, such as Simmental, Uckermark, and Aubrac, are almost identical from 4 to 22 weeks of gestation in comparison with Holstein cattle, although there are concentration differences thereafter (Shahin et al. 2014), suggesting that the profile of serum PAGs S-N values in Japanese Black cattle is similar to that of other beef cattle. Serum PAGs concentrations in Holstein, Angus, and Brangus breeds at about 60 days of gestation have been reported to temporarily decrease to approximately half the concentration at 30–32 days of gestation. However, the cause remains unknown (Sasser et al., 1986; Thompson et al., 2010; Mercadante et al., 2013; Ricci et al., 2015). In this study, a temporary decrease in serum PAGs S-N values was also observed in Japanese Black cattle, but to a lesser extent than in other breeds. Differences in blood PAGs concentrations have been associated with breed (Shahin et al., 2014), subspecies (Mercadante et al., 2013; Fontes et al., 2019), and crossbred bull differences (Franco et al., 2018). Furthermore, breed differences are associated with increased foetal weight, organ, muscle, and body fat weights during the second and third trimesters of gestation (Mao et al., 2008). It is possible that breed differences in blood PAGs concentrations are related to foetal developmental status and differences in the molecular species of genetically expressed PAGs (Green et al., 2000).

Serum E_1S concentrations gradually increased from 70 days, increased significantly from 250, peaked at 280, and then decreased at 285 days after AI. Previous studies have reported that blood E_1S concentrations start detecting around 100 days of gestation, gradually increase as pregnancy progresses, peak approximately 10 days before calving, and then decrease (Takahashi et al., 1997; Patel et al., 1999; Zhang et al. 1999). The serum E_1S concentrations in this study showed a similar profile.

The birth weight of the offspring was moderately positively correlated with the AUC of serum PAGs S-N values and E_1S concentrations between 100 and 250 days and between 150 and 285 days after AI, respectively. The $\geq$ 37 kg group had higher mean serum PAGs S-N values at 150 and 200 days and higher mean serum E_1S concentrations at 280 and 285 days after AI than the $<$ 37 kg group. Thus, monitoring serum PAGs S-N values in the second trimester could be used to select dams with larger calf birth weights earlier than serum E_1S concentrations and may be a parameter to predict the possibility of dystocia due to excessive foetal size. In mid-pregnancy, the placenta undergoes extensive remodelling and shape changes to facilitate rapid foetal growth and development (Bertolini et al., 2004; Estrella et al., 2017). Many authors have highlighted the relationship between PAGs synthesis and placental health (Patel et al., 1997; Mercadante et al., 2013), and it is believed that PAGs in the blood play an important role in placental remodelling during pregnancy (Barbato et al., 2022). Therefore, the positive

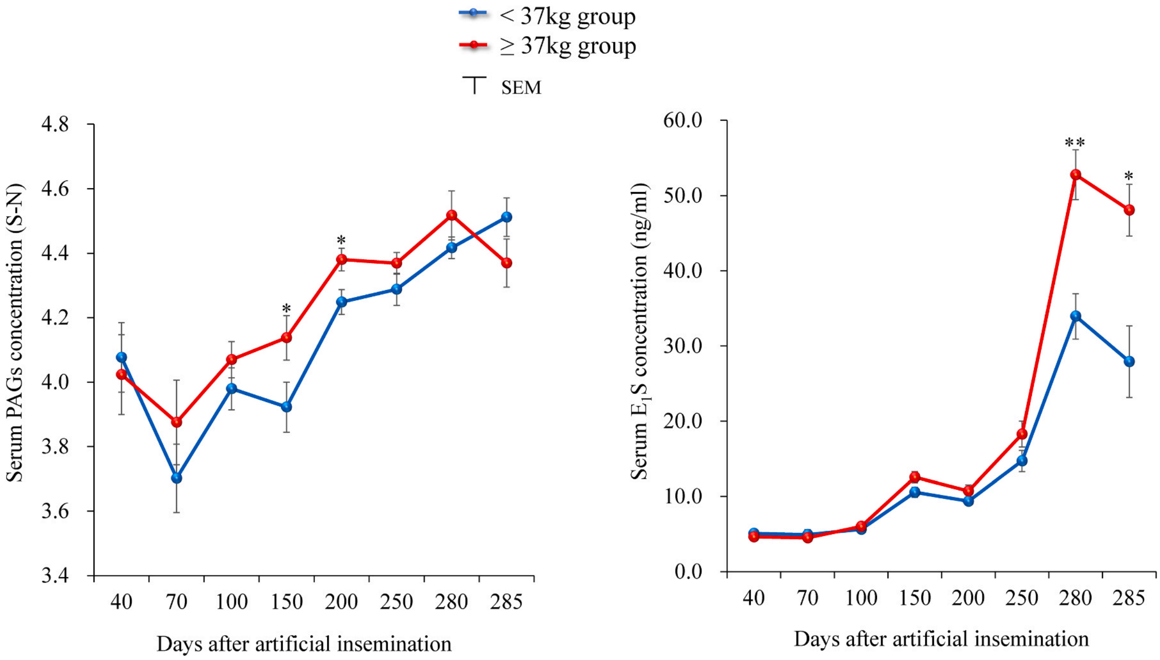

Fig. 3. Comparison of pregnancy-associated serum glycoproteins (PAGs) S-N values and estrone sulphate (E_1S) concentrations in groups with calf birth weight under 37 kg (< 37 kg group) and equal to or over 37 kg (≥ 37 kg group).Data are presented as mean ± standard error of the mean (SEM).* Significant difference ($P < 0.05$) ** Significant difference ($P < 0.01$).

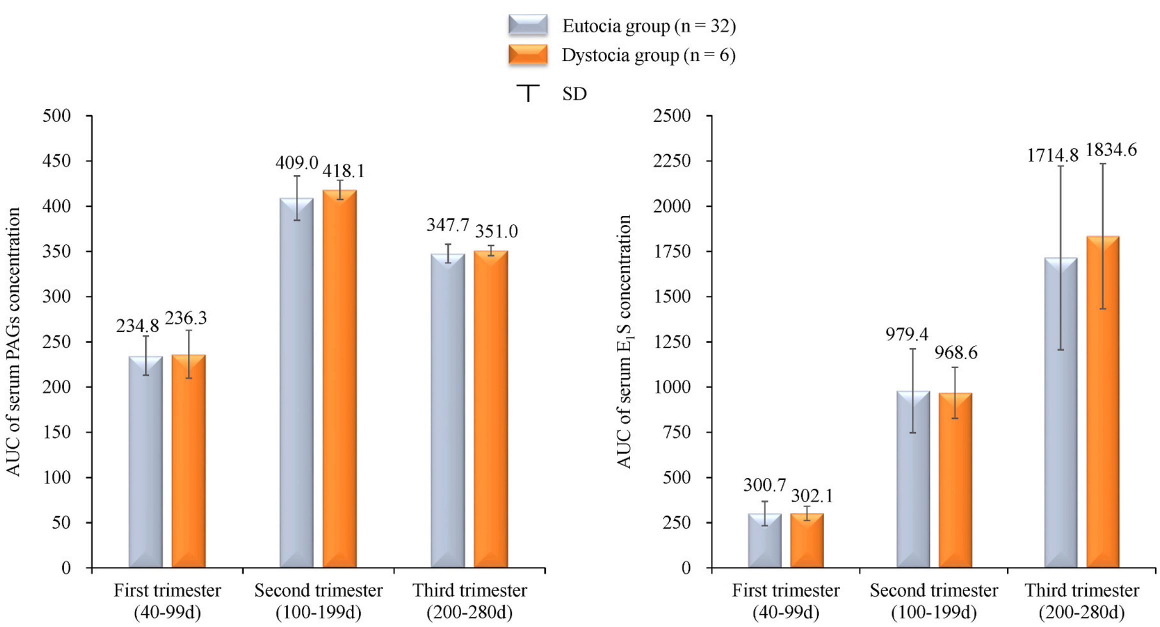

Fig. 4. Comparison of area under the curve (AUC) of serum pregnancy-associated glycoproteins (PAGs) S-N values and estrone sulphate (E_1S) concentrations in eutocia and dystocia groups. First trimester, 40–99 days after artificial insemination. Second trimester, 100–199 days after artificial insemination. Third trimester, 200–280 days after artificial insemination. Data are presented as mean ± standard deviation (SD).

correlation between serum PAGs S-N values in the second trimester and birth weight of the offspring in this study suggests that this may be affected by placental remodelling to match the birth weight of the offspring.

Although the AUC of serum PAGs S-N values in the second trimester and serum E_1S concentrations in the third trimester were larger in the dystocia group, there was no significant difference between the two groups. It may be necessary to take into accounts the size of the dam's pelvis, because dystocia is influenced not only by foetal factors but also by maternal factors, and in particular, dystocia due to excessive foetal size is also influenced by the size of the dam's pelvis (Maeda et al., 2022).

The ratio of the change in serum E_1S concentrations at each blood collection time point was calculated based on 70 days after AI, and it was greater in the dystocia group from 70 to 280 days after AI. Therefore, the ratio of the change in serum E_1S concentrations from 70 to 280 days after AI may be a parameter for predicting dystocia. The crown-rump length and body weight of the foetus increase slightly until approximately 100 days of gestation, and then develop rapidly (Bauman and Currie, 1980; Okano, 1994). All dystocia groups had birth weights >

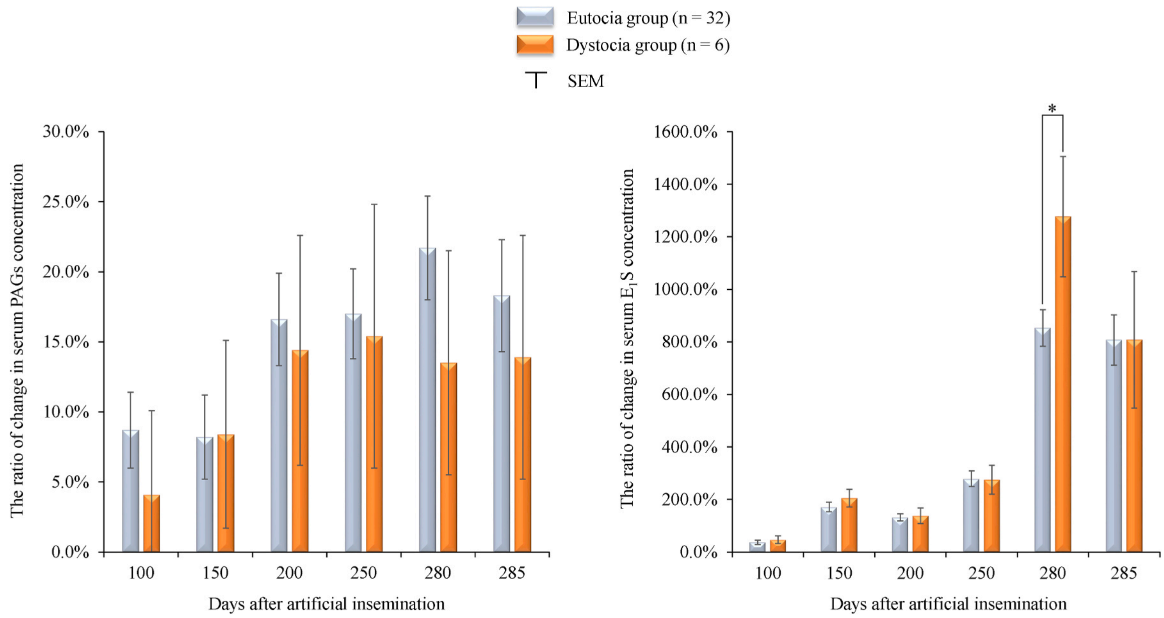

Fig. 5. Comparison of the ratio of change in serum pregnancy-associated glycoproteins (PAGs) S-N values and estrone sulphate (E_1S) concentrations between 70 days after artificial insemination (AI) and each blood sampling in eutocia and dystocia groups. The ratio of change was calculated based on 70 days after AI [(each concentration - the concentration at 70 days after AI) / the concentration at 70 days after AI × 100]. Data are presented as mean ± standard error of the mean (SEM). * Significant difference ($P < 0.05$).

37 kg, and the birth weights of the dystocia group were larger than those of the eutocia group, suggesting that foetal growth was greater after 70 days of AI, resulting in a larger ratio of change at 280 days to 70 days.

The present study suggests that blood PAGs S-N values in the second trimester and the ratio of change in blood E_1S concentrations at 70 and 280 days after AI may be a new parameter for predicting dystocia. Although it was not possible to establish a method for predicting dystocia based on this number of cows, all of them were assisted by two or three farm employees with calving equipment, and were defined as severe cases with a large degree of foetus overweight in relation to the maternal pelvis. Therefore, these six cases are valuable as baseline data for identifying factors that may predict dystocia, and we believe that the changes in PAGs S-N values in mid-pregnancy and E_1S concentration in late pregnancy in this study provide parameters that may be useful for establishing a new method of predicting dystocia. In addition, the present study provided data on eutocia cows, which is also necessary for predicting dystocia in the future.

The most important factor in beef cattle management is the healthy growth of the foetus during pregnancy and subsequent successful births. Therefore, if serum PAGs and E_1S concentrations in pregnant cattle can be used to predict dystocia, calf productivity can be improved. However, practical application of the parameters obtained in this study requires trials with a larger number of dystocia cases. In addition, compared to previously reported methods for predicting dystocia, such as measurement of foetal metacarpal/metatarsal width (Takahashi et al., 2005) or foetal hoof width (Maeda et al., 2022) immediately before calving, monitoring of the PAGs and E_1S levels requires sampling of at least two points, and cannot detect morphological abnormalities or malposition of the foetus. Nevertheless, it would be possible to establish an accurate method of predicting dystocia by finding factors other than PAGs and E_1S that could be candidates for the method.

5. Conclusions

Serum PAGs S-N values in the second trimester of pregnancy could be applied to identify dams at risk for greater birth weight of the offspring earlier than serum E_1S concentrations, suggesting that serum E_1S concentrations, along with the ratio of change at 280 days to 70 days post-AI, may be a new parameter for predicting dystocia.

CRediT authorship contribution statement

Takafumi Maeda:Writing – original draft, Visualization, Resources, Methodology, Investigation, Formal analysis, Data curation. Takeshi Osawa:Writing – review & editing, Supervision, Project administration, Funding acquisition, Conceptualization. Go Kitahara:Writing – review & editing, Validation, Supervision, Resources, Methodology, Conceptualization.

Declaration of Competing Interest

None of the authors have any financial or personal relationships that could inappropriately influence or bias the content of this paper.

Acknowledgements

The authors are grateful to IDEXX Laboratories, Inc. (Koganei, Tokyo, Japan) for conducting serum PAGs S-N values measurements. This study was supported by a Grant-in-Aid for the Promotion of the Livestock Industry from the Japan Racing Association (Project No. 2021-33).

References

Barbato, O., Menchetti, L., Brecchia, G., Barile, V.L., 2022. Using Pregnancy-Associated Glycoproteins (PAGs) to improve reproductive management: From dairy cows to other dairy livestock. Animals 12, 2033.
Bauman, D.E., Currie, W.B., 1980. Partitioning of nutrients during pregnancy and lactation: a review of mechanisms involving homeostasis and homeorhesis. Journal of Dairy Science 63, 1514–1529.
Bellows, D.S., Ott, S.L., Bellows, R.A., 2002. Cost of reproductive diseases and conditions in cattle. the Professional Animal Scientist 18, 26–32.
Bertolini, M., Moyer, A.L., Mason, J.B., Batchelder, C.A., Hoffert, K.A., Bertolini, L.R., Carneiro, G.F., Cargill, S.L., Fumula, T.R., Sainz, R.D., et al., 2004. Evidence of increased substrate availability to in vitro-derived bovine foetuses and association with accelerated conceptus growth. Reproduction 128, 341–354.
Bragg, R., Macrae, A., Lycett, S., Burrough, E., Russell, G., Corbishley, A., 2021. Risk factor analysis for beef calves requiring assisted vaginal delivery in Great Britain. Veterinary Record 188, e6.

Dunlap, K.A., Brown, J.D., Keith, A.B., Satterfield, M.C., 2015. Factors controlling nutrient availability to the developing fetus in ruminants. Journal of Animal Science and Biotechonology 6, 16.

Echternkamp, S.E., 1993. Relationship between placental development and calf birth weight in beef cattle. Animal Reproduction Science 32, 1–13.

Estrella, C.A.S., Kind, K.L., Derks, A., Xiang, R., Faulkner, N., Mohrdick, M., Fitzsimmons, C., Kyuk, Z., Grutzner, F., Roberts, C.T., et al., 2017. Remodelling of the bovine placenta: Comprehensive morphological and histomorphological characterization at the late embryonic and early accelerated fetal growth stages. Placenta 55, 37–46.

Fontes, P.L.P., Oosthuizen, N., Ciriaco, F.M., Sanford, C.D., Canal, L.B., Pohler, K.G., Henry, D.D., Mercadante, V.R.G., Timlin, C.L., Ealy, A.D., et al., 2019. Impact of fetal vs. maternal contributions of *Bos indicus* and *Bos taurus* genetics on embryonic and fetal development. Journal of Animal Science 97, 1645–1655.

Franco, G.A., Peres, R.F.G., Martins, C.F.G., Reese, S.T., Vasconcelos, J.L.M., Pohler, K. G., 2018. Sire contribution to pregnancy loss and pregnancy-associated glycoprotein production in Nelore cows. Journal of Animal Science 96, 632–640.

Green, J.A., Xie, S., Quan, X., Bao, B., Gan, X., Mathialagan, N., Beckers, J.F., Roberts, R. M., 2000. Pregnancy-associated bovine and ovine glycoproteins exhibit spatially and temporally distinct expression patterns during pregnancy. Biology of Reproduction 62, 1624–1631.

Hirako, M., Takahashi, T., Domeki, I., 2002. Peripheral changes in estrone sulfate concentration during the first trimester of gestation in cattle: comparison with unconjugated estrogens and relationship to fetal number. Theriogenology 57, 1939–1947.

Isobe, N., Nakao, T., Uehara, O., Yamashiro, H., Kubota, H., 2003. Plasma concentration of estrone sulfate during pregnancy in different breeds of Japanese beef cattle. Journal of Reproduction and Development 49, 369–374.

Johanson, J.M., Berger, P.J., 2003. Birth weight as a predictor of calving ease and perinatal mortality in Holstein cattle. Journal of Dairy Science 86, 3745–3755.

Kanda, Y., 2013. Investigation of the freely available easy-to-use software 'EZR' for medical statistics. Bone Marrow Transplantation 48, 452–458.

Maeda, T., Kitahara, G., Osawa, T., 2022. Establishment of a method to predict dystocia due to physical imbalance between foetus and maternal pelvis in Japanese Black cattle. Reproduction in Domestic Animals 57, 1029–1037.

Mao, W.H., Albrecht, E., Teuscher, F., Yang, Q., Zhao, R.Q., Wegner, J., 2008. Growth- and breed-related changes of fetal development in cattle. Asian-Australasian Journal of Animal Sciences 21, 640–647.

Mekonnen, M., Moges, N., 2016. A review on dystocia in cows. European Journal of Biological Sciences 8, 91–100.

Mercadante, P.M., Waters, K.M., Mercadante, V.R.G., Lamb, G.C., Elzo, M.A., Johnson, S. E., Rae, D.O., Yelich, J.V., Ealy, A.D., 2013. Subspecies differences in early fetal development and plasma pregnancy-associated glycoprotein concentrations in cattle. Journal of Animal Science 91, 3693–3701.

Miguel-Pacheco, G.G., Curtain, L.D., Rutland, C., Knott, L., Norman, S.T., Phillips, N.J., Perry, V.E.A., 2017. Increased dietary protein in the second trimester of gestation increases live weight gain and carcass composition in weaner calves to 6 months of age. Animal 11, 991–999.

Northrop, E.J., Rich, J.J.J., Rhoades, J.R., Perry, G.A., 2019. Comparison of two bovine serum pregnancy tests in detection of artificial insemination pregnancies and pregnancy loss in beef cattle. PLOS ONE 14, e0211179.

Ogata, Y., Abe, H., Misawa, T., Takahashi, K., Ban, A., Katoh, T., Sakai, J., 1995. Relationship between perinatal death and birth weight in Japanese Black calves. Journal of Reproduction and Development 41, j77–j81.

Okano, A., 1994. Lifelong reproductive performance and fetal development in Japanese black cows. Journal of Reproduction and Development 40, j117–j129.

Patel, O.V., Sulon, J., Beckers, J., Takahashi, T., Hirako, M., Sasaki, N., Domeki, I., 1997. Plasma bovine pregnancy-associated glycoprotein concentrations throughout gestation in relationship to fetal number in the cow. European Journal Endocrinology 137 423–428.

Patel, O.V., Takenouchi, N., Takahashi, T., Hirako, M., Sasaki, N., Domeki, I., 1999. Plasma oestrone and oestradiol concentrations throughout gestation in cattle: relationship to stage of gestation and fetal number. Research in Veterinary Science 66, 129–133.

Redifer, C.A., Duncan, N.B., Meyer, A.M., 2021. Factors affecting placental size in beef cattle: maternal and fetal influences. Theriogenology 174, 149–159.

Reynolds, L.P., Borowicz, P.P., Caton, J.S., Vonnahme, K.A., Luther, J.S., Hammer, C.J., Carlin, K.R.M., Grazul-Bilska, A.T., Redmer, D.A., 2010. Developmental programming: the concept, large animal models, and the key role of uteroplacental vascular development. Journal of Animal Science 88, E61–E72.

Ricci, A., Carvalho, P.D., Amundson, M.C., Fourdraine, R.H., Vincenti, L., Fricke, P.M., 2015. Factors associated with pregnancy-associated glycoprotein (PAG) levels in plasma and milk of Holstein cows during early pregnancy and their effect on the accuracy of pregnancy diagnosis. Journal of Dairy Science 98, 2502–2514.

Roberts, J.N., May, K.J., Veiga-Lopez, A., 2017. Time-dependent changes in pregnancy-associated glycoproteins and progesterone in commercial crossbred sheep. Theriogenology 89, 271–279.

Sakatani, M., Sugano, T., Higo, A., Naotsuka, K., Hojo, T., Gessei, S., Uehara, H., Takenouchi, N., 2018. Vaginal temperature measurement by a wireless sensor for predicting the onset of calving in Japanese Black cows. Theriogenology 111, 19–24.

Sasaki, Y., Uematsu, M., Kitahara, G., Osawa, T., Sueyoshi, M., 2014. Effects of stillbirth and dystocia on subsequent reproductive performance in Japanese Black cattle. The Veterinary Journal 200, 462–463.

Sasser, G.R., Ruder, C.A., Ivani, K.A., Butler, J.E., Hamilton, W.C., 1986. Detection of pregnancy by radioimmunoassay of a novel pregnancy-specific protein in serum of cows and a profile of serum concentrations during gestation. Biology of Reproduction 35, 936–942.

Schwartz, S., Pateman, T., 2021. Pre-clinical Pharmacokinetics. In: A Handbook of Bioanalysis and Drug Metabolism, First Ed. CRC Press, Boca Raton, FL, USA, pp. 113–131.

Shahin, M., Friedrich, M., Gauly, M., Holtz, W., 2014. Pregnancy-associated glycoprotein (PAG) profile of Holstein-Friesian cows as compared to dual-purpose and beef cows. Reproduction in Domestic Animals 49, 618–620.

Simões, J., Stilwell, G., 2021. Normal Birth (Eutocia). In: Calving Management and Newborn Calf Care, First Edn. Springer, Cham, pp. 51–79.

Sullivan, T.M., Micke, G.C., Magalhaes, R.S., Phillips, N.J., Perry, V.E.A., 2009. Dietary protein during gestation affects placental development in heifers. Theriogenology 72, 427–438.

Takahashi, M., Goto, T., Tsuchiya, H., Ueki, A., Kawahata, K., 2005. Ultrasonographic monitoring of nuclear transferred fetal weight during the final stage of gestation in Holstein cows. Journal of Veterinary Medical Science 67, 807–811.

Takahashi, T., Hirako, M., Takahashi, H., Patel, O.V., Takenouchi, N., Domeki, I., 1997. Maternal plasma estrone sulfate profile during pregnancy in the cow; comparison between singleton and twin pregnancies. Journal of Veterinary Medical Science 59, 287–288.

Thompson, I.M., Cerri, R.L.A., Kim, I.H., Green, J.A., Santos, J.E.P., Thatcher, W.W., 2010. Effects of resynchronization programs on pregnancy per artificial insemination, progesterone, and pregnancy-associated glycoproteins in plasma of lactating dairy cows. Journal of Dairy Science 93, 4006–4018.

Uematsu, M., Sasaki, Y., Kitahara, G., Sameshima, H., Osawa, T., 2013. Risk factors for stillbirth and dystocia in Japanese Black cattle. The Veterinary Journal 198, 212–216.

Weldeyohanes, G., Fesseha, H., 2020. Dystocia in domestic animals and its management. International Journal of Pharmacy & Biomedical Research 7, 1–11.

Wooding, F.B.P., 2022. The ruminant placental trophoblast binucleate cell: an evolutionary breakthrough. Biology of Reproduction 107, 705–716.

Zhang, W.C., Nakao, T., Moriyoshi, M., Nakada, K., Ribadu, A.Y., Ohtaki, T., Tanaka, Y., 1999. Relationship of maternal plasma progesterone and estrone sulfate to dystocia in Holstein-Friesian heifers and cows. Journal of Veterinary Medical Science 61, 909–913.