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Assessing Serum Vaspin Dynamics in Dairy Cows during Late Pregnancy and Early Lactation in Relation to Negative Energy Balance

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Abstract: The periparturient period, which spans late pregnancy to early lactation in dairy cows, is a crucial phase characterized by complex metabolic and endocrine adjustments necessary for sustained milk production. This research focused on the relationship between serum vaspin, inflammatory cytokines (IL-1, TNF), and markers of negative energy balance (NEB) in 100 primiparous and multiparous Holstein dairy cows. The results demonstrated that one month post-calving, both groups had a significant decrease in serum vaspin levels but increased NEFA levels, indicating possible consequences for lipid metabolism and energy balance. Multiparous cows showed significant elevations in cholesterol, IL-1, and TNF concentrations after calving, indicating increased inflammatory responses. Primiparous cows, on the other hand, responded differently, indicating the role of parity in metabolic adjustments. The study acknowledges limitations such as sample size and its observational nature. Future research should investigate the long-term effects of these metabolic changes on herd health and lactational performance, using advanced technologies to gain a molecular understanding. Despite limitations, this study provides valuable insights into how adipokines, inflammatory markers, and energy balance interact during the periparturient period, offering the potential for improved dairy cow management and productivity while ensuring animal welfare.

Keywords: dairy cows; early lactation; milk production; negative energy balance; pregnancy; serum vaspin

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1. Introduction

Dairy cows undergo significant physiological changes during late pregnancy and early lactation, transitioning from a negative to a positive energy balance [1]. A negative energy balance (NEB) arises when cows cannot consume enough energy to support milk production, leading to the mobilization of body fat reserves [2]. NEB is a common challenge in dairy farming, impacting cow health, fertility, and milk production [3]. To enhance dairy cow management practices and welfare, it is essential to understand factors influencing NEB, such as serum vaspin dynamics [4].

Serum vaspin, an emerging adipokine, is believed to affect energy metabolism and insulin sensitivity in various species, including humans and rodents [5]. However, its role in dairy cows, especially during the transition period, remains unclear. Investigators, veterinarians, and dairy farmers may find it advantageous to analyze serum vaspin dynamics in these animals during the later stages of pregnancy and the early lactation period in order to enhance the welfare, health, and productivity of dairy cows [6].

Dairy cows go through significant metabolic changes during this time [7]. Fetal development causes cows to consume less dry matter in late pregnancy, which might result in NEB. Consequently, NEB is made worse by the higher energy need for producing milk during the early stages of lactation [8]. Increased body fat mobilization is linked to these metabolic alterations, which may lead to metabolic diseases such fatty liver syndrome and ketosis [9].

It is imperative to understand the metabolic changes that occur during the transition phase; yet, little is known about the role of serum vaspin in dairy cows [4]. The fluctuations of serum vaspin in dairy cows over late gestation and the initial phase of lactation, particularly its relationship to non-epidermal banding (NEB), are not well studied. Completing these data gaps will be essential to comprehending how vaspin affects energy metabolism and insulin sensitivity, two aspects that have an impact on the welfare and productivity of cattle [10]. Since this research offers prospective biomarkers for the early detection of metabolic disorders such fatty liver syndrome and ketosis, it has significant implications for the management and welfare of dairy cows [9]. Improved management practices could lessen the detrimental impacts of NEB on cow productivity and health. Understanding the relationship involving serum vaspin levels and NEB might additionally clarify the metabolic changes that take place at this critical point, which could guide future studies and management strategies in the dairy sector [11].

Vaspin, TNF-alpha, and IL-1 are the primary biomarkers linked to immune response and inflammation in animals, particularly dairy cows. Two inflammatory disorders in dairy cows associated with higher levels of these indicators are fatty liver syndrome (FLS) and ketosis [12]. Secondly, Non-esterified fatty acids (NEFAs) demonstrate the impact on cows' lipid metabolism. Increased levels of NEFA are frequently linked to metabolic diseases including ketosis and FLS since adipose tissue mobilizes fatty acids excessively. Lastly, lipids and lipoproteins play a major role in lipid transport and metabolism. Deviant lipid profiles, characterized by changes in lipoprotein concentrations and lipid composition, have been observed in cows with FLS and ketosis [13–15].

Understanding the complex interactions among vaspin, inflammatory markers, and lipid profiles could lead to tailored nutritional and healthcare interventions, promoting sustainable and economically viable practices in the dairy industry.

2. Materials and Methods

2.1. Study Protocol and Implementation

The current study was conducted in two separate dairy herds located in the Al-Qadisiyah provinces of Southern Iraq (Latitude: 32.04369100, Longitude: 45.14945050), with ethical approval granted by the College of Veterinary Medicine, University of Al-Qadisiyah, prior to commencing animal experimentation (Protocol Number: VMCP-ref: 34/2023).

The operational protocols and management standards were uniformly maintained for both herds [16]. One hundred Holstein dairy cows were chosen for their diverse parity statuses and underwent close scrutiny one month preceding and succeeding parturition. Cows were divided into two groups: primiparous (n = 46, with an average age of 2.1 ± 0.1 years) and multiparous (n = 54, with an average age of 4.3 ± 0.8 years). The cows' body condition was evaluated at the start of the study using the American Virginia system modified by Edmonson [17], which employs a finely graded scale ranging from 1 (indicating thinness) to 5 (reflecting obesity), with increments of 0.25. Cows with body condition scores ranging from 3 to 3.75 were included in the study [18]. Reassessment of body condition scores was performed upon the study's culmination. Pre-parturition housing comprised open-shed barns, which seamlessly transitioned to free-stall barns post-parturition. The milking schedule was conducted twice daily to track the average daily milk yield during the initial two months of lactation for both groups of cows: primiparous and multiparous. Health screenings ensured the overall health of all participants, confirming the absence of internal and external parasites. The dietary regimen encompassed a mix of grass hay, grass silage, and concentrate. The nutritional composition of the diets administered during the steaming-up period and subsequent early lactation is outlined in Table 1.

Table 1. Nutritional composition of cows in late pregnancy and early lactation periods.

Diet Component	Late Pregnancy		Postpartum	
	Size (gm)	**Percentage (%)**	**Size (gm)**	**Percentage (%)**
Grass Hay	500	50	600	60
Grass Silage	300	30	180	18
Concentrate	200	20	220	22

Nutritional Composition

Component	Late Pregnancy Ration (kg/day)	Postpartum Ration (kg/day)
Dry Matter	0.55	0.70
Crude Protein	0.12	0.14
Crude fiber	0.20	0.18
Fat	0.05	0.06
Ash	0.08	0.07
Calcium	0.015	0.012
Phosphorous	0.008	0.009
Magnesium	0.003	0.004
Potassium	0.020	0.018
Sodium	0.003	0.002
Sulfur	0.002	0.0015
Iron	0.002	0.0025
Manganese	0.001	0.0012
Zinc	0.0005	0.0006
Copper	0.0003	0.00035
Selenium	0.0001	0.00015
Vitamin A	100 IU	120
Vitamin D	10 IU	15
Vitamin E	0.2 IU	0.25
Vitamin K	0.1 IU	0.12
Thiamin	0.002	0.0025
Riboflavin	0.004	0.0045
Niacin	0.006	0.007
Pantothenic acid	0.005	0.0055
Vitamin B6	0.003	0.0032
Folate	0.001	0.0011
Vitamin B12	0.2	0.25
Choline	0.15	0.06

2.2. Blood Sampling

Blood samples were collected one month pre and post-parturition by puncturing the coccygeal vein using a vacutainer tube vacupuncture tube without anticoagulant. This timing was selected for the assessment of changes in the measured parameters before and after calving. In this study, the first sampling was conducted at the expected date of parturition. The actual dates of parturition varied slightly from the expected dates, with some cows calving earlier or later than anticipated. The average deviation recorded from the expected parturition date is 5 days (range: 2–8 days). This variability in timing of parturition was taken into account in the current study to ensure accurate estimation of physiological change pre and post- calving.

The blood samples were allowed to coagulate at 25 °C/15 min, allowing the serum to naturally separate. Then, to acquire clean serum samples, centrifugation was performed for 10 min at 3000× g. Following that, the serum was collected and stored at −20 °C pending the next analytical step [19].

2.3. Measurement of Blood Hormones and Metabolites

Serum vaspin levels were determined using a specific bovine ELISA Kit (BIOTANG Inc., Lexington, MA, USA) [20]. The assay's precision was ensured with intra- and inter-assay coefficients of variation of 3.6% and 7.4%, respectively. Vaspin levels can be accurately and sensitively detected with a spectrum of detection of 0.2–5 ng/mL. TNF-α and IL-1 levels in serum were measured using ELISA kits from SunLong Biotech Co., LTD, Hangzhou, China. Owing to stringent quality control protocols, the variation between the intra- and inter-assay coefficients were 6.1% and 8.5%, respectively. This dependable technology allowed for the precise measurement of TNF-α and IL-1 levels in serum samples [21]. The levels of Non-Esterified Fatty Acids (NEFA) in serum were estimated via ELISA test using A commercial kits obtained from Randox Laboratories, Crumlin, UK [22]. Serum triglyceride (TRIG), cholesterol, low-density lipoprotein (LDL), and high-density lipoprotein (HDL) levels were measured using commercial kits from Pars Azmoon Co., Tehran, Iran [23].

2.4. Statistical Analyses

Statistical analyses were carried out employing GraphPad Prism 8 software (La Jolla, CA, USA) [24]. Data was displayed as mean ± standard deviation (SD) to demonstrate the central tendency as well as the variability clearly. The Kolmogorov-Smirnov test was used to determine data normality, while Levene's test was used to verify variance homogeneity. These checks were crucial to ensuring the validity of subsequent statistical analyses. Repeated measures analysis was used to examine the impact of sampling time, parity, and their interaction (time × parity) on serum concentrations of metabolic factors. Parity had two levels as the between-subjects factor, and sampling time had two levels as the within-subjects factor. A general linear model was employed to analyze complex relationships in the data. Post hoc analyses were conducted using the least significant difference (LSD) test to identify specific differences between groups. Pearson's correlation coefficients were calculated to investigate relationships between serum vaspin levels and other relevant factors, providing insights into potential associations in the dataset. The significance level was set to $p < 0.05$ to ensure that observed effects and correlations were statistically meaningful. This rigorous approach ensured the robustness of statistical findings.

3. Results

3.1. Milk Production and Body Condition

One month after calving, milk production reached 35.6 ± 14.10 kg/day for primiparous cows and 39.6 ± 3.95 kg/day for multiparous cows. No significant difference in body condition score (BCS) was observed between primiparous (3.35 ± 1.33) and multiparous dairy cows (3.35 ± 0.10) compared to prepartum values (Figure 1). Additionally, the total dry matter intake (DMI) was 10.32 kg/day.

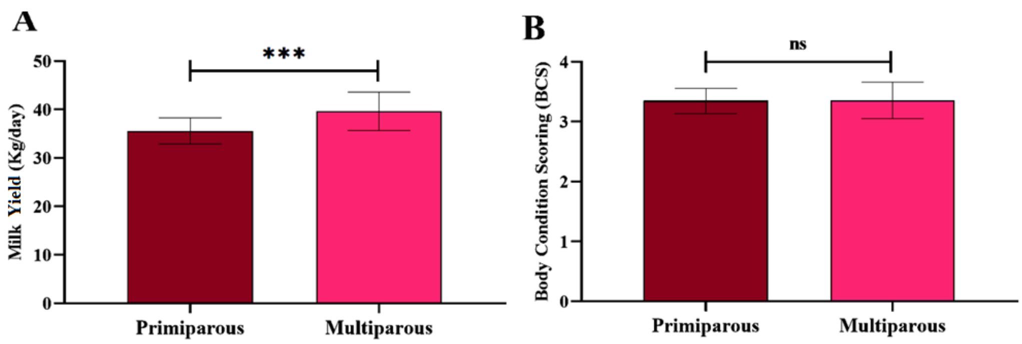

Figure 1. Comparison of (**A**) milk Yield (Kg/day) and (**B**) body condition scores in primiparous and multiparous dairy cows one month after calving. (***): statistically significant; (ns): non-significant.

3.2. Metabolic and Endocrine Factors

Differences in Changes Pre- and Post-Calving

Table 2 displays the levels of metabolic and endocrine factors in dairy cows during late pregnancy and early lactation. Parity did not influence the concentrations of serum vaspin, non-esterified fatty acids (NEFAs), triglycerides (TG), cholesterol, low-density lipoprotein

(LDL), and high-density lipoprotein (HDL) one month before calving. However, after calving, both primiparous and multiparous cows showed increased levels of serum NEFA and IL-1 compared to pre-calving levels.

Table 2. Concentrations of metabolic and endocrine factors in dairy cows pre- and post-calving.

Metabolic Factor	Pre-Calving		Post-Calving	
	Primiparous (Mean ± SD)	Multiparous (Mean ± SD)	Primiparous (Mean ± SD)	Multiparous (Mean ± SD)
NEFA (Mm)	0.5 ± 0.076^{b}	0.4 ± 0.066^{b}	0.6 ± 0.095^{a}	0.6 ± 0.097^{a}
Vaspin (ng/mL)	0.7 ± 0.08^{d}	0.7 ± 0.084^{c}	0.5 ± 0.054^{b}	0.6 ± 0.073^{a}
Cholesterol (mg/dL)	123.9 ± 13.737^{b}	119.6 ± 14.754^{b}	130.7 ± 13.603^{a}	140.9 ± 20.166^{a}
TG (mg/dL)	21.8 ± 0.766^{b}	24.0 ± 5.282^{a}	29.1 ± 6.433^{a}	26.1 ± 4.286^{a}
HDL (mg/dL)	63.2 ± 7.451^{a}	60.1 ± 8.476^{a}	62.0 ± 6.463^{a}	65.5 ± 6.398^{a}
LDL (mg/dL)	56.4 ± 16.323^{b}	54.6 ± 8.027^{b}	62.9 ± 12.791^{a}	70.2 ± 21.893^{a}
IL-1 (pg/dL)	89.2 ± 8.982^{c}	83.1 ± 10.487^{c}	97.99 ± 15.842^{b}	111.95 ± 22.744^{a}
TNF-α (pg/dL)	266.2 ± 23.285^{c}	213.7 ± 37.418^{c}	226.9 ± 20.793^{b}	254.5 ± 49.271^{a}

The different small letter (a–d) indicte statistical significant differences ($p < 0.05$) between groups; The same letter indicate non-significant differences ($p > 0.05$).

Compared to pre-calving values, Table 2 illustrates significant changes after calving, including a decrease in serum vaspin and an increase in NEFAs in both primiparous and multiparous cows. Cholesterol, IL-1, and TNF levels significantly increased after calving in multiparous cows, with no significant differences observed in primiparous cows. Serum TG, HDL, and LDL levels showed no significant differences before and after parturition in primiparous and multiparous cows.

3.3. Correlation Analyses

Before calving, there was a strong negative correlation between vaspin and IL-1 (Pearson R = −0.907, $p < 0.0001$) and vaspin and TNF (Pearson R = −0.566, $p < 0.001$). However, the correlation between vaspin and NEFA was insignificant (Pearson R = −0.023, $p > 0.05$). Post-calving, the correlation between vaspin and IL-1 remained significant but was now positive (Pearson R = 0.478, $p < 0.01$), indicating a change in the correlation direction. Similarly, the correlation between vaspin and TNF also remained significant post-calving, but was now positive (Pearson R = 0.340, $p < 0.05$). The correlation between vaspin and NEFA post-calving was also positive, but insignificant (Pearson R = 0.253, $p > 0.05$) (Table 3).

Table 3. Correlation analysis of serum vaspin with inflammatory factors and NEFAs in dairy cows pre- and post-Calving.

Serum Factor	Pre-Calving		Post-Calving	
	Pearson R	*p*-Value	Pearson R	*p*-Value
Vaspin vs. IL-1	−0.907	<0.0001 ***	0.478	<0.01 *
Vaspin vs. TNF	−0.566	<0.001 **	0.340	<0.05 *
Vaspin vs. NEFA	−0.023	>0.05	0.253	>0.05

p *: *p*-value < 0.05–0.01 considered significant; **, ***: *p*-value < 0.001–0.0001 is considered highly significant.

The current study results revealed that before calving, there was an insignificant positive correlation ($p > 0.05$) between serum vaspin and the levels of cholesterol, TG, HDL, and LDL. Similarly, after calving, there was no significant correlation ($p > 0.05$) observed between these parameters. However, the correlation between vaspin and TG differed, displaying a negative association instead of a positive one (Table 4).

Table 4. Correlation analysis of serum vaspin with lipid profile components in dairy cows before and after calving.

Serum Factor	Pre-Calving		Post-Calving	
	Pearson R	*p* Value	Pearson R	*p* Value
Vaspin vs. Cholesterol	0.061	0.709	0.115	0.481
Vaspin vs. TG	0.247	0.087	−0.291	0.068
Vaspin vs. HDL	0.021	0.896	0.136	0.403
Vaspin vs. LDL	0.23	0.887	0.018	0.913

4. Discussion

This study focused on the metabolic and endocrine fluctuation in dairy cows during the late pregnancy and early lactation periods, through estimation of serum vaspin, inflammatory cytokines (IL-1, TNF), and lipid profiles, with consequences for optimizing management strategies during the periparturient phase. The current study reported that one month post calving, primiparous cows produced an average of 35.6 ± 14.10 kg/day, in contrast multiparous cows yielded 39.6 ± 3.95 kg/day indicating a distinguish difference in milk yielding between multiparous and primiparous cows during the early lactation phase. The predicted milk production plateau aligns with the standard hypothesis that primiparous cows produce lower milk than multiparous cows [25]. This pattern is congruent with the physiological development of mammary glands in primiparous cows, which is frequently associated with higher milk supply during early lactation [26]. However, it is important to recognize that differences in management approaches, genetics, and environmental factor can influence outcomes across different research [27]. The present study showed no significant alterations in the body condition score (BCS) between primiparous (3.35 ± 1.33) and multiparous dairy cows (3.35 ± 0.10) compared to prepartum values [28,29]. Stated differently, the BCS of the two groups of cows did not change during the prepartum phase, indicating that their nutritional condition was stable prior to calving. This evidence was important because it suggests that cows, whether primiparous or multiparous, might make the shift from late gestation to early lactation and yet remain physically fit [30,31]. According to the current findings, employing the proper nutritional factors in herds provided consistent BCSs, which most likely improved the cows' overall health and wellbeing [32].

The present study emphasizes the importance of considering a variety of factors that influence body composition and milk production, encouraging further research into these basic principles in order to gain comprehensive knowledge. Before breastfeeding, parity was found to have no effect on serum vaspin, cholesterol, triglycerides (TG), non-esterified fatty acids (NEFA), low-density lipoprotein (LDL), or high-density lipoprotein (HDL). Based on this observation, metabolic parameters are steady before calving, which is in accordance with other studies reporting that metabolic profiles in the later stages of pregnancy may not alter considerably between parity groups [33–35].

It's noteworthy to observe that multiparous and primiparous cows had greater blood NEFA and IL-1 levels than pre-calving cows [28]. Dairy cows with NEFA levels of approximately 0.6 mM are thought to be increased, particularly in the vicinity of calving and maybe at DIM 30, because of the metabolic alterations and negative energy balance that are commonly seen during this time. NEFA levels can rise as a result of body fat stores being continuously mobilized to fulfill energy demands, indicating metabolic stress and perhaps raising health concerns for cows [36]. Furthermore, after calving, serum vaspin concentrations dropped in both groups. Surprisingly, after giving birth, primiparous cows had lower tumor necrosis factor (TNF) levels than their multiparous counterparts, who showed higher TNF levels. This discovery may point to differences in immune system control or inflammatory processes between primiparous (first-time calving) and multiparous (repeated calving) cows [37]. Extensive research on the fundamental processes influencing these variations in TNF levels can yield important understandings of the physiological distinctions between primiparous and multiparous cows in the post-calving phase. Comprehending these variations can aid in enhancing management techniques and the general well-being and health of dairy herds [10].

Previous research has also revealed consistent findings regarding steady metabolic parameters prior calving in dairy animals under optimal management [38,39]. In both parity groups, NEFA levels increased after calving, which was consistent with the expected metabolic changes during the early stages of lactation [40]. Given that vaspin is known to be involved in metabolic control, the surprising drop in serum vaspin levels in both groups after calving warrants more research and examination. Its decrease could be attributed to the metabolic needs of lactation, highlighting the need for additional research on this topic [41,42]. Changes in immunological status or stress levels during lactation may result in changes in how primiparous and multiparous cows respond to TNF [43,44]. The decrease in serum vaspin concentrations implies that adipokine responds to nutritional requirements during lactation, which was confirmed by earlier investigations [6]. More investigations are required to determine the precise mechanisms causing this drop and the possible consequences for metabolic regulation during the early stages of lactation. Similarly, improved fatty acid mobilization is linked to higher postnatal NEFA levels as well as metabolic alterations during the early stages of lactation.

Postpartum inflammatory and adipose profiles related to energy balance in multiparous cows exhibited substantial rises in TNF, IL-1, and cholesterol levels. These variations in reactions between groups of cows highlight the influence associated with factors such as stress levels and duration of lactation [45]. The lack of significant differences in TG, HDL, and LDL cholesterol concentrations prior to and following delivery in both parity groups is consistent with research showing the consistency of lipid profiles over the periparturient period under optimum management conditions. Future research must take these aspects into account as variations in lipid metabolism may be influenced by them. These factors include diet composition and metabolic health [46]. The correlation study gave important insights into the link between blood vaspin levels and numerous metabolic markers in dairy cows during late pregnancy and early lactation [47]. Significantly negative associations were found before calving between the proinflammatory markers TNF and IL-1, suggesting that vaspin may have an anti-inflammatory role in late pregnancy. In contrast, it appears that vaspin does not directly affect the regulation of lipid metabolism prior to calving because there is no significant link with non-esterified fatty acids [23]. Further evidence for a possible link between vaspin and lipid homeostasis was found before parturition in non-significant positive correlations between vaspin and lipid profile elements such as cholesterol, triglycerides (TG), high-density lipoprotein (HDL), and low-density lipoprotein (LDL).

The pre-calving results align with earlier studies suggesting that vaspin may have anti-inflammatory effects in late pregnancy [6]. The lack of association observed with NEFAs suggests that vaspin might not have a direct impact on lipid metabolism prior to calving. However, substantial positive correlations with TNF and IL-1 during the early stages of breastfeeding point to a shift in the regulatory role of vaspin, possibly indicating its involvement in proinflammatory processes during this time [44]. The correlations with lipid profiles in the early stages of lactation highlight the intricate relationship between vaspin and lipid metabolism and highlight the need for further research to fully understand its function in complex metabolic changes during the periparturient phase.

5. Conclusions

This study examines metabolic and endocrine changes in dairy cows during the transition from late pregnancy to early lactation. Results show that one month after calving, both primiparous and multiparous cows experienced decreased serum vaspin levels and increased non-esterified fatty acids (NEFAs). Additionally, cholesterol, interleukin-1 (IL-1), and tumor necrosis factor (TNF) levels increased post-calving in multiparous cows, with distinct responses in primiparous cows. These findings highlight the complex interaction between adipokines, inflammatory markers, and lipid metabolism during this period. The study emphasizes the influence of parity, suggesting tailored management strategies for primiparous and multiparous cows. Limitations include the sample size and temporal scope, suggesting the need for future studies to capture individual variations and dynamic changes throughout early lactation. The observational nature of the study also presents challenges in establishing causal relationships, warranting further experimental designs. Additionally, dietary composition and environmental factors, though controlled to an extent, may introduce confounding variables. The study lays the groundwork for future research to understand the mechanisms governing the periparturient period in dairy cows and explore long-term implications for health and lactational performance. Investigating the regulatory roles of vaspin in inflammation and lipid metabolism during late pregnancy and early lactation may identify therapeutic targets for optimizing energy balance and immune responses in dairy cows. Understanding molecular pathways could be improved by incorporating cutting-edge technologies like omics techniques. All things considered, this research advances dairy farming's precision management by offering suggestions for improving cow welfare and the sustainability of the sector.

Author Contributions: H.A.N. and A.G.R. were responsible for conceptualizing the study and conducting formal analyses. N.K.H.A. and H.A.-K. contributed to the methodology and validation of the study. H.A.N. and N.K.H.A. curated the data and created visualizations. H.A.-K. and A.G.R. participated in writing the initial draft of the manuscript. All authors contributed to the writing, reviewing, and editing of the manuscript. H.A.-K. supervised the project. All authors have read and agreed to the published version of the manuscript.

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Informed Consent Statement: Not applicable.

Data Availability Statement: Data used to support the findings of this study are available from the corresponding author upon request.

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