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Colegiado de Pós-Graduação em Zootecnia

FATORES ASSOCIADOS À MORTALIDADE, MORBIDADE E DESEMPENHO DE BEZERRAS EM ALEITAMENTO

MATHEUS BALDUINO MOREIRA

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Dissertação apresentada ao programa de pós-graduação em Zootecnia da Escola de Veterinária da Universidade Federal de Minas Gerais, como requisito parcial para obtenção de grau de Mestre em Zootecnia.

Área de concentração: Produção Animal.

Orientadora: Sandra Gesteira Coelho

Coorientadora: Camila Stefanie de Oliveira

Coorientadora: Fernanda Carolina Ferreira

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ATA DE DEFESA DE DISSERTAÇÃO DE MATHEUS BALDUINO MOREIRA

Às 08:00h do dia 11 de dezembro de 2019, reuniu-se, na Escola de Veterinária da UFMG a Comissão Examinadora de Dissertação, indicada pelo Colegiado na reunião do dia 09/07/2019 para julgar, em exame final, a defesa da dissertação intitulada. FATORES ASSOCIADOS À MORTALIDADE, MORBIDADE E DESEMPENHO DE BEZERRAS EM ALEITAMENTO, como requisito final para a obtenção do Grau de **Mestre em Zootecnia, área de Concentração em Produção Animal.**

Abrindo a sessão, o Presidente da Comissão, Prof.ª Sandra Gesteira Coelho, após dar a conhecer aos presentes o teor das Normas Regulamentares da Defesa de Dissertação, passou a palavra ao candidato (a), para apresentação de seu trabalho. Seguiu-se a arguição pelos examinadores, com a respectiva defesa do(a) candidato(a). Logo após, a Comissão se reuniu, sem a presença do(a) candidato(a) e do público, para julgamento da dissertação, tendo sido atribuídas as seguintes indicações:

	Aprovada	Reprovada
Prof. (a)/Dr.(a) HELTON MATTANA SATURNINO	X	
Prof. (a)/Dr.(a) Elias Jorge Facury Filho	X	
Prof. (a) /Dr. (a) SANDRA GESTEIRA COELHO	X	
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Para concluir o Mestrado, o(a) candidato(a) deverá entregar 08 volumes encadernados da versão final da dissertação, acatando, se houver as modificações sugeridas pela banca, e a comprovação de submissão de pelo menos um artigo científico em periódico recomendado pelo Colegiado dos Cursos. Para tanto terá o prazo máximo de 60 dias a contar da data da defesa.

O resultado final, foi comunicado publicamente ao(a) candidato(a) pelo Presidente da Comissão. Nada mais havendo a tratar, o Presidente encerrou a reunião e lavrou a presente ata, que será assinada por todos os membros participantes da Comissão Examinadora e encaminhada juntamente com um exemplar da dissertação apresentada para defesa.

Belo Horizonte, 11 de 12 de 2019.

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EPÍGRAFE

"Só sabemos com exatidão quando sabemos pouco; à medida que vamos adquirindo conhecimentos, instalam-se as dúvidas."

Johann Goethe

Dedico,

À minha grande família e amigos.

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SUMÁRIO

LISTA DE ILUSTRAÇÕES

LISTA DE ABREVIAÇÕES

CG	Composição genética
DAD	Incidência de Doenças Antes do Desaleitamento
DBN	Diarreia bovina neonatal
DEA	Dias em aleitamento
DRB	Doença respiratória bovina
EE	Extrato etéreo
ENA	Estação de nascimento do animal
GPDd	Ganho de peso diário ao desaleitamento
GPT	Ganho de peso ao desaleitamento
IgG	Imunoglobulina G
IPD	Idade a primeira doença
NM	*Net Merit*
OPR	Ordem de parto da receptora
PB	Proteína bruta
PD	Peso no desaleitamento
PGA	Período de gestação do animal
PH	Predominante Holandês
PN	Peso ao nascimento
PTA Milk	*Predicted Transmitting Ability Milk*
PTS	Proteína total sérica
PZ	Predominante zebu
RPM	Retenção de placenta na mãe
TIP	Transferência de imunidade passiva
TPB	Tristeza parasitária bovina
VPN	Valor Preditivo Positivo
VPP	Valor Preditivo Negativo

RESUMO

A criação de novilhas representa um grande custo para as fazendas leiteiras, mas os dados sobre os fatores de risco para falha na transferência da imunidade passiva (FTIP) em países tropicais são escassos. Nosso objetivo foi descrever os fatores de risco para FTIP e investigar como essa se associa ao risco de morbidade, mortalidade e crescimento de bezerros em aleitamento de duas composições genéticas em condições tropicais. Realizamos um estudo de coorte retrospectivo e utilizamos dados pré e pós-nascimento em nível de bezerras. Foram 6.011 bezerras mestiças em aleitamento de um único rebanho, nascidas entre 2012-2018. Obtivemos informações sobre a genealogia dos bezerros, a estação de nascimento, a ocorrência de retenção de placenta (RP), proteína sérica total (PTS), morbidade (diarreia neonatal de bezerros - DNB, doença respiratória bovina - DRB e tristeza parasitária bovina - TBP), mortalidade e ganho de peso. A composição genética foi dividida em predominantemente Gir leiteiro (PG, raça Holandesa 0-50%), e predominantemente Holandês (PH, raça Holandesa> 50%). Foi realizada regressão logística mista multivariada (SAS 9.4). Os pontos de corte ideais do PTS para predizer morbidade e mortalidade foram 7,6 g / L e 6,9 g / L, respectivamente. O valor médio do PTS foi de 7,2 g / L. Nos pontos de corte de 5,2 g / L, 7,6 g / L e 6,9 g / L, a prevalência de FTIP foi de 2%, 55% e 31%. As bezerras PH tiveram uma chance 1,35 maior de ter FTIP e 1,48 maior de ter alguma doença. As bezerras nascidas de vacas multíparas e de partos seguidos de RP apresentaram maior chance de FTIP. No geral, a prevalência da doença foi de 53%, e 41% das bezerras tinham DNB, 18% tinham DRB, 10% tinham TBP. A estação do ano, a ordem de parto da mãe, a capacidade de transmissão prevista pelo pai para produção de leite (PTA leite) e o peso ao nascimento também foram associados à probabilidade de doença. FTIP não foi um bom preditor de doença. A taxa de mortalidade geral foi de 6%. As bezerras PH tiveram uma chance 2,99 maior para mortalidade do que as bezerras PG. O risco de mortalidade variou de acordo com uma interação entre FTIP e a estação de nascimento, mas bezerras de touros com PTA positivo para leite tiveram maior chance de morrer. O ganho médio diário foi de 0,636, e bezerras com FTIP (ponto de corte de 5,2 g / L) ganharam menos peso do que bezerras sem FTIP. Uma transferência adequada de imunidade passiva pode não ser suficiente para prevenir a morbidade e mortalidade se as bezerras forem criadas em condições desafiadoras.

Palavras chaves: Falha de transmissão da imunidade passiva, diarreia neonatal dos bezerros, doença respiratória bovina e tristeza parasitária bovina.

ABSTRACT

Heifer rearing represents a large cost for dairy enterprises, but data on risk factors for failure of transfer of passive immunity in tropical countries is scarce. Our objective was to describe risk factors for failure of transfer of passive immunity (FTPI) and to investigate how FPTI is associated with the risk of morbidity, mortality, and growth of pre-weaned dairy calves from two genetic compositions in tropical conditions. We performed a retrospective cohort study and used pre- and post-birth calf-level data from 6,011 crossbred pre-weaned calves from a single herd, born between 2012-2018. We obtained information on calf pedigree, the season of birth, the occurrence of retained placenta (RP), total serum protein (TSP), morbidity (neonatal calf diarrhea - NCD, bovine respiratory disease - BRD, and tick-borne disease - TBD), mortality, and weight gain. The genetic composition was predominantly dairy Gyr (**PG**, 0-50% Holstein breed), and predominantly Holstein (**PH**, > 50% Holstein breed). Multivariate mixed logistic regression was performed (SAS 9.4). The optimal TSP cut-off points for predicting morbidity and mortality were 7.6 g/L and 6.9 g/L, respectively. The median value of TSP was 7.2 g/L. At cut-off points of 5.2 g/L, 7.6 g/L, and 6.9 g/L the prevalence of FTPI was 2%, 55%, and 31%. PH calves had 1.35 greater odds of having FTPI, and 1.48 greater odds of disease. Calves born from multiparous cows and from calving followed by RP had greater odds of FTPI. Overall, the prevalence of disease was 53%, and 41% of the calves had NCD, 18% had BRD, 10% had TBD. Season, parity order of the dam, sire predicted transmitted ability for mil (PTA milk), and weight at birth were also associated with odds of disease. FTPI was not a good predictor of disease. The overall mortality rate was 6%. Calves PH had 2.99 greater odds of mortality than PG. The mortality risk varied according to an interaction between FTPI and the season of birth, but calves from sires with a positive PTA for milk had greater odds of dying. The average daily gain was 0.636, and calves with FTPI (cut-off point of 5.2 g/L) gained less weight than calves without FTPI. An adequate transfer of passive immunity may not be enough to prevent morbidity and mortality if calves are raised in challenging conditions.

Keywords: failure of transfer of passive immunity, neonatal calf diarrhea, bovine respiratory disease, cattle tick fever.

CAPÍTULO 1 – REVISÃO DE LITERATURA

1. INTRODUÇÃO

A criação de animais jovens é o segundo maior custo dentro dos sistemas de produção de leite brasileiros e a ineficiência na sua condução, por vezes, pode levar ao insucesso das fazendas leiteiras. Fatores como alta morbidade e alta mortalidade, com consequente baixo desempenho, além de aumentar os custos de produção no curto prazo, contribuem com a ineficiência dos animais adultos no longo prazo. Descobertas recentes também demonstram que o estresse térmico durante o final a gestação compromete a saúde e a produção futura das crias (Monteiro et al., 2016).

A produção brasileira de leite é estimada em 33,5 bilhões de litros anuais, sendo o quarto maior produtor mundial (ONU, 2018). O Estado de Minas Gerais concentra a maior produção de leite do Brasil, sendo responsável por 27% do volume total produzido. A produção no estado é caracterizada pela grande variabilidade quanto ao tamanho dos rebanhos e sistemas de produção, estes têm como padrão racial predominante o gado mestiço de Holandês x Zebu (FAEMG, 2006).

Poucos estudos descrevem a realidade do rebanho jovem brasileiro, dados sobre desempenho, morbidade e mortalidade são pouco conhecidos. O conhecimento dos números e sua utilização como *benchmarking* é importante na determinação do sucesso das fazendas leiteiras. Assim, determinar estes números é de grande importância para a cadeia produtiva do leite.

Os objetivos gerais deste estudo foram (1) levantar os principais indicadores de produtividade (2) a epidemiologia das doenças e (3) mortalidade na criação de bezerras pré-desmama. O objetivo específico foi determinar como diversos fatores se inter-relacionam influenciando os parâmetros descritos nos objetivos gerais.

2. REVISÃO BIBLIOGRÁFICA

2.1. Transferência de imunidade passiva

A placenta dos bovinos classifica-se como sindesmocorial, que apresenta o benefício de proteger o feto contra a maioria das ações microbianas, entretanto impede a passagem de proteínas séricas de alto peso molecular, como as imunoglobulinas (Ig), da circulação materna para a fetal. Dessa forma, as bezerras nascem agamaglobulinêmicas e precisam ingerir colostro para adquirir tal proteção. A transferência de imunidade passiva (TIP) é um processo que visa passar a memória imunológica da vaca para o bezerro, seu insucesso, a falha de transmissão da imunidade passiva (FTIP), pode aumentar a morbidade e a mortalidade até 3 meses de idade (Winderyer et al., 2014; Shivley et. al., 2018a), que compromete o desempenho nessa categoria (Shivley et al., 2018b).

Define-se como FTIP a concentração de imunoglobulinas (IgG) menor que 10 mg/ml no plasma de uma bezerra entre 24 e 48 horas de vida (Godden, 2008). Entretanto, outros estudos mostram que os bezerros são mais resistentes a infecções respiratórias, quando atingem concentrações de IgG acima de 15 mg/ml (Furman-Fratczak et al., 2011). Outros trabalhos já sugerem alterar em definitivo o ponto de corte para 15 mg/ml (Urie et al., 2018).

Inúmeras são as variáveis determinantes para o sucesso da TIP em uma fazenda leiteira, a quantidade e qualidade do colostro oferecido implicam na massa de IgG colostral consumida, bem como o tempo entre o nascimento e a administração do colostro alteram a absorção de anticorpos (Morin et al., 1997, Shivley et al., 2018a).

Os principais fatores que interferem na qualidade do colostro foram descritos por Godden (2008) como sendo: idade da mãe, nutrição no período pré-parto, volume de colostro produzido, colostro proveniente de quartos com mastite, programa de vacinação, duração do período seco e o tempo entre parto e a ordenha do colostro. Neste mesmo trabalho também foram elencados fatores que interferem na absorção pelo neonato: tempo entre o parto e o fornecimento, método de alimentação, presença da mãe, distúrbios metabólicos, estresse pelo frio e contaminação bacteriana do colostro.

O método ouro para determinação da concentração plasmática de IgG é a imunodifusão radial (Calloway et al., 2002; Deelen et al., 2014; Elsohaby et al., 2015) porém outros métodos são utilizados como: determinação da proteína total sérica (PTS) por refratometria, por sulfato de zinco e turbidez do sulfito de sódio; testes de coagulação de gluteraldeído e mensuração da atividade da g-glutamil transferase (Calloway et al., 2002). Nas fazendas, os de maior destaque são a determinação da PTS (Calloway et al., 2002) e mais recentemente avaliação de BRIX (Deelen et al., 2014; Elsohaby et al., 2015), ambos obtidos com a ajuda de refratômetros específicos.

Durante anos, a literatura científica apoiou a realização da PTS em bezerros dentro de 24-48 horas após o nascimento, como sendo o período ideal para realização do procedimento. Trabalho recente, conduzido por Wilm et al. (2018) foi realizado para avaliar momento ideal para se determinar a PTS em bezerros Holandês. Quando comparados com o momento 24 após o nascimento, a maior correlação foi observada nos dias 2 e 3 (r = 0,99 e 0,98) após o nascimento, se mantendo elevada entre os dias 4 e 9 (r = 0,88) com declínio somente a partir do dia 10 (r = 0,76). Esses resultados suportam o maior período para avaliação do soro para determinação da TIP, o que facilita a rotina nas propriedades leiteiras.

Uma vastidão de trabalhos trata do tema TIP ao longo do tempo (Morin et al., 1997). Trabalhos alicerçam o papel fisiológico, as diversas variáveis críticas no processo (Godden, 2008), as consequências do manejo inadequado (Winderyer et al., 2014; Shivley et. al., 2018a) e atestam a aplicabilidade de metodologias para aferição no ambiente de fazendas (Calloway et al., 2002; Deelen et al., 2014; Elsohaby et al., 2015). Entretanto, a grande maioria destes trabalhos foram realizados em sistemas de produção de gado Holandês e em países de clima temperado. Desta forma, estudos contemplando a realidade brasileira são necessários.

2.2. Morbidade e mortalidade em bezerras leiteiras

Inúmeros fatores têm sido relacionados em influenciar na mortalidade e morbidade na fase de pré-desmama. Dentre os principais fatores se encontram: técnica de biotecnologia da reprodução utilizada (Siqueira et. al. 2017), taxa de natimortos, tamanho do rebanho (Winder et. al. 2018), tempo de permanência da mãe com a cria (Vogels et al. 2013), estação do ano do nascimento (Santman Berends et. al. 2019), intervenção ao parto (Murray et al., 2015), estresse calórico da mãe no pré-parto (Kelley, 1982; Dahl et al., 2016), peso ao nascimento (Winderyer et al., 2014), FTIP (Furman-Fratczak et al., 2011) e entre outros.

Trabalho importante avaliando fazendas americanas participantes do *National Animal Health Monitoring System's Dairy* (NAHMS) foi conduzido por Urie et al., (2018). Os pesquisadores realizaram análises descritivas dos dados de morbidade e mortalidade de 2.545

bezerras na fase de aleitamento nos anos de 2014 e 2015. Segundo a equipe de pesquisa, sinais clínicos relacionados a problemas digestivos foram os mais recorrentes, aparecendo em 17,2% dos animais estudados, representando 50,9% dos bezerros doentes e 43,6% de todos os casos. Sinais clínicos relacionados a problemas respiratórios, associação de respiratórios e digestivos e outros sinais representaram 9,5%, 1,8% e 8,0%, respectivamente, do total de bezerros doentes, representando 27,0%, 4,6% e 24,8% do total de casos, respectivamente. A mortalidade foi de 5% no período pré-desmama, sendo registradas 128 mortes do total de bezerros acompanhados. Após o diagnóstico pós-morte as principais causas foram: 32% por afecções digestivas; 14,1% por respiratórias; 7,0% pela associação de digestivas e respiratórias; 13,3% por outras causas (injúrias, infecções, bezerros vendidos sem razão específica); 25% por causas desconhecidas e 8,6% não tiveram anotações relativas à morte.

No mesmo trabalho os pesquisadores realizaram análise multivariada dos dados para determinação dos fatores que mais interferiram na morbidade e mortalidade nessa fase. No modelo final proposto para morbidade, o peso ao nascimento ($P = 0,004$), concentração sérica de IgG ($P = 0,001$), tipo de ventilação utilizada no bezerreiro ($P = 0,015$) e índice de temperatura e umidade no mês pré-parto ($P = 0,008$), foram significativos. Para mortalidade, as variáveis significativas foram, peso ao nascimento ($P = 0,011$), concentração sérica de IgG ($P = 0,004$), quantidade de gordura (kg) oferecida na dieta líquida ($P = 0,011$) e morbidade no período pré-desmama ($P = 0,001$).

No levantamento de práticas de saúde e gestão de fazendas leiteiras americanas (USDA, 2018), as perdas com natimortos alcançam valores de 6% das bezerras que nascem. Além disso, a mortalidade e o descarte pré-desmame giram em torno de 6,0% e 0,4%, respetivamente, e de 1,7% e 0,2% após o desmame, respectivamente. Durante a fase de aleitamento, as diarreias e outros problemas digestivos são as principais ocorrências que acometem essa categoria, sendo responsáveis por 56,4% destas baixas enquanto os problemas respiratórios são responsáveis por 24,0%. Após a desmama, os problemas respiratórios são as ocorrências com maior destaque, 56,4% sobre o total de mortes, seguidos de injúrias, 13,5%. As causas desconhecidas na fase pré e pós desmame são respectivamente 5,6 e 11,4%, representando grande importância no número de mortes. Lombard et al. (2019) demostraram a importância da determinação correta das causas das mortes para estabelecimentos de práticas de gestão adequadas propondo um método sistemático para anotações nas criações de bezerras. Este método consiste em um diagrama que possuiu perguntas de sim ou não em diversos níveis até chegar a possível causa.

Trabalho semelhante foi conduzido em outras regiões do mundo como Canadá e Holanda. Winder et al. (2018) levantaram a mortalidade pré e pós-desmama no Canadá por meio da utilização de questionários. Os pesquisadores relataram valores de 6,4 e 2,4%, respectivamente, para o ano de 2014. Na Holanda, Santman Berends et.al., (2019) avaliaram os dados de mortalidade até um ano de idade dos animais, sendo dividido em três fases: até os 14 dias (3,3%), de 15 a 55 dias (4,5%) e de 56 dias até um ano (3,1%), os autores relataram 10,9% do total de nascimento até um ano de vida.

Em 2019 a empresa IDEAGRI, utilizando o *software* brasileiro IDEAGRI®, criou o Índice Ideagri do Leite Brasileiro (IILB,2019) realizado com dados de um *software* brasileiro (IDEAGRI®). O objetivo da criação deste índice foi caracterizar a pecuária leiteira brasileira. Foram utilizados dados de cerca de 900 propriedades em universo superior a 3.000, para determinar alguns indicadores zootécnicos. Neste índice, a sobrevivência de bezerras até um ano de idade foi de 84%, número inferior as médias de outros países e preocupante, visto que se trata de propriedades com grande emprego de tecnologia. Este mesmo levantamento, determinou as maiores causas de mortalidade no rebanho jovem até um ano. Para a análise dos dados, foram consideradas somente as propriedades com mais de 70% das causas de morte informadas, desconsiderando assim as propriedades com causas "desconhecidas" e "outras" com somas superiores a 30%. O número total de fazendas utilizadas na análise foi de 360, e as principais causas de morte nas propriedades foram: diarreia (21,0%), tristeza parasitária bovina (20,4%), pneumonia (14,3%), outras (7,2%), desconhecidas (6,2%).

No levantamento de dados realizado no Brasil (IILB,2019), foi observado um elevado número de causas de mortes não definidas (6,2%). Interessantemente, Winder et al., (2018) conduzindo trabalho no Canadá, também relataram alto número de mortes por causas desconhecidas. Esses números altos são preocupantes uma vez que, não ajudam na orientação de novas práticas de manejo e pesquisas.

Assim, maior atenção será dada nessa revisão as três maiores causas de mortalidade nos rebanhos brasileiros que são: problemas digestivos, tristeza parasitária bovina e problemas respiratórios.

2.2.1. Diarreia neonatal bovina

Em um estudo sobre fatores associados a morbidade, mortalidade e crescimento, Winderyer et al., (2014), descreveram a epidemiologia da diarreia neonatal bovina (DNB) e os fatores associados a essa. A incidência de DNB foi de 21,2% antes de 2 semanas de idade (608/2874), 1,8% entre 2 e 5 semanas (52/2874) e 0,35% entre 5 semanas e 3 meses (10/2874). Mais de 23% dos animais foram tratados pelo menos uma vez (670/2784) e 8,7% foram tratados mais de uma vez (58/670), sendo que o primeiro caso aconteceu em média aos 10 dias (0 a 71 dias de intervalo). Na análise multivariada, o baixo peso ao nascimento, estação do ano (primavera e verão) e incidência de outras doenças contribuíram significativamente para maior incidência de DNB.

Abuelo et al. (2019), em investigação sobre práticas de manejo em bezerros leiteiros na Austrália determinaram também etiologia da DNB. Participaram da pesquisa 106 fazendas, sendo que 55,7% dos produtores enviaram amostras de fezes diarreicas para determinação dos agentes. O principal patógeno isolado foi *Cryptosporidium parvum,* sendo isolado em 64,4% das fazendas, seguido por *Salmonella entérica* (52,5%), *rotavírus* (49,1%), *coronavírus* (40,7%) e *E.coli* (35,6%). Foram analisadas 202 amostras e a idade média do caso foi 1,3 $\pm$ 5,29 dias. Foram positivas para somente um agente 70 amostras (34,7%), 76 amostras (37,6%) foram positivas para 3 agentes, 33 (16,3%) foram positivas para 3 ou mais agentes e 23 amostras (11,4%) foram negativas para os agentes pesquisados. O *Cryptosporidium ssp.* foi isolado em 40,9%, *Salmonella ssp.* em 25,2%, *rotavírus* em 19,1%, *E. coli* em 13,9% e o *coronavírus* 7,4%. Neste mesmo trabalho o início da diarreia aconteceu 64,1% das vezes de 6 a 21 dias e 32,1% das vezes de 0 a 5 dias de idade.

2.2.2. Doença respiratória bovina

A doença respiratória bovina (DRB) é um grande problema para produtores de leite tanto para o gado jovem quanto para o gado adulto. Fatores como FTIP, cura do umbigo, tipo de alojamento, ventilação, alimento utilizado na dieta líquida, estresse na desmama, programa de vacinação contribuem no aumento da incidência da doença (Gorden e Plummer, 2010).

Winderyer et al. (2014), descreveram a epidemiologia da DRB. Dos animais avaliados 21,9% foram tratados pelo menos uma vez (630/2874) e 19,4% foram tratados mais de uma vez (122/630), sendo que o primeiro caso aconteceu em média aos 30 dias (1 a 111 dias de intervalo). A incidência foi de 7,7% antes de 2 semanas de idade (221/2874), 8% entre 2 e 5 semanas

(229/2874) e 9,5% entre 5 semanas e 3 meses (273/2874). A estação de nascimento (inverno e verão), ser do quartil de maior risco entre os rebanhos, ausência de cura de umbigo, incidência de outras doenças e ter recebido antibiótico na primeira semana de vida tiveram efeito no aumento de incidência da DRB.

Um estudo longitudinal conduzido por Dubrovsky et al., (2019) relatou práticas que podem ser modificadas para diminuir o risco de DRB em animais em aleitamento. A prevalência média entre os rebanhos foi de 22,8%. Foram considerados fatores de proteção o uso de leite, de descarte ou comercializável, em comparação com sucedâneo; aleitamento de 3,8 litros por bezerro até os 21 dias de vida; troca frequente de cama da maternidade e administração de vacinas modificadas vivas ou mortas contra DRB nas mães no pré-parto. Já o uso de casinhas com telhados metálicos, partos gemelares e áreas de criação com presença de poeira foram considerados fatores de risco para a ocorrência da DRB.

2.2.3. Tristeza parasitária bovina

A tristeza parasitária bovina (TPB), também conhecida como doença do carrapato, é uma doença hemolítica causada por uma Rickettsia, *Anaplasma marginale* e os protozoários, *Babesia bigemina* e *babesia bovis*. No Brasil, é a segunda maior causa de mortalidade (20,4%) em bovinos até um ano de idade, ficando atrás da DNB (21%) e sendo mais importante que a DRB (14,3%) (IILB,2019).

Os dados de TPB são escassos na literatura científica. Trabalho conduzido por Oliveira Júnior et al., (2018), avaliaram métodos eletrônicos para auxiliar no diagnóstico precoce da enfermidade. Os pesquisadores observaram a ocorrência do primeiro caso da doença aos 125 ± 16 dias com o peso de 119 ± 19 kg. Moreira (2017), observou, em um rebanho em Minas Gerais, a idade ao primeiro caso de 125 ± 19 dias, variando entre 106 e 139 dias nas diversas composições raciais. A frequência de apresentação clínica da TPB foi de 46%, variando de 13 a 65% entre as composições raciais. Neste trabalho, a estação de nascimento, a composição genética e a idade ao desaleitamento apresentaram influência sobre a frequência de TPB clínica.

2.3. Desempenho produtivo

Inúmeros fatores causam prejuízo no desempenho produtivo dos animais no pré-desmame, dentre eles, FTIP e morbidade. Os impactos negativos no desempenho vão desde a pré-desmama (Dahl et al., 2016; Shivley et al., 2018b) até as lactações futuras (Faber et al., 2005; Soberon e Van Amburg; 2014), passando pela puberdade (Dahl,2016).

Trabalhando com bancos de dados do NAHMS, Shivley et al. (2018b), por meio de modelos multivariados, estudaram os principais fatores que influenciam no desenvolvimento pré-desmama de bezerras leiteiras. No modelo, as variáveis avaliadas *status* sanitário (P < 0,001), quantidade em kg de proteína na dieta líquida (P = 0,004), oferecimento de leite pasteurizado ou não (P < 0,001), adição de probióticos (P = 0,123), houve interação entre uso de leite pasteurizado e adição de probióticos (P < 0,001), índice de temperatura e umidade no pré-parto (P < 0,001), número de lactações da mãe (P < 0,001), tipo de cama (P < 0,001), partos simples versus gemelares (P = 0,007), excreção fecal de *Cryptosporidium* (P = 0,003), e excreção fecal de *Giardia* (P = 0,020) foram significativas.

Fatores relacionados ao bem-estar animal, passaram a ser alvos de estudos na literatura científica mundial. Trabalho conduzido por Dahl et al. (2016), avaliaram o desempenho de bezerros nascidos de mães submetidas ou não a estresse térmico no pré-parto. Ambos os lotes de vacas eram mantidos em instalações tipo *free stall* e a única diferença era que de um lado da instalação as mães eram resfriadas e do outro não eram. As mães resfriadas apresentaram temperatura retal entre 0,3 e 0,4°C abaixo das mães não resfriadas. Bezerras filhas de mães estressadas no pré-parto apresentaram menor peso ao nascimento (39,1 ± 0,7 x 44,8 ± 0,7 kg - P < 0,01), à desmama e aos 12 meses de idade (190,9 ± 3,7 x 200,2 ± 3,4 kg - P < 0,05), porém o peso ao parto não diferiu em relação as filhas de mães resfriadas. Assim sendo, o menor peso ao nascimento resultou em menor tamanho corporal, mas não comprometeu o peso ao parto, o que pode ser explicado por alterações no metabolismo que propiciam maior acúmulo de gordura.

No mesmo trabalho relatado no parágrafo anterior (Dahl et al., 2016) também foi relatado os impactos na puberdade e produtividade na primeira lactação de bezerras estressadas no útero no final da gestação. Novilhas que passaram por estresse térmico tiveram concepção de 38,5% contra 55,5% do grupo não estressado e produção média de leite 5,1 litros inferior nas primeiras 35 semanas de lactação.

Outro fator que traz impactos no desempenho ao longo da vida produtiva é a TIP. Faber et al. (2005), forneceram 2 ou 4 litros de colostro entre 50 e 140 mg de Ig/ml para bezerras Pardo Suíço na primeira alimentação. Após este manejo, todos os outros cuidados dispensados foram idênticos. Apesar de não terem feito a aferição de eficiência de colostragem encontraram diferenças favoráveis ao grupo que recebeu 4 litros de colostro ao nascimento. O ganho de peso até a concepção foi maior (1,03 ± 0,03 x 0,80 ± 0,02 kg; $P < 0,001$) e a produção de leite ajustada aos 305 dias também (9.907 ± 335 e 11.294 ± 335 kg x 8.952 ± 341 e 9.642 ± 341 kg na primeira e segunda lactação, respectivamente).

Soberon e Van Amburgh (2013), realizaram Meta Análise envolvendo 12 artigos científicos, os autores relataram que a produção de leite na primeira lactação foi maior quando houve aumento da ingestão de nutrientes do leite ou substituto do leite pelas bezerras durante a fase de aleitamento. No mesmo artigo, esses autores elaboraram uma Meta-Regressão onde se relacionou o ganho de peso na fase de aleitamento com a produção de leite na primeira lactação. Eles demostraram que para cada quilo de ganho de peso pré desmama acima de 250 gramas a produção de leite na primeira lactação aumentou em 1.550 kg.

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Título do projeto: Manejo de novilhas leiteiras em fazendas do estado de Minas Gerais: “Fatores associados à morbidade, mortalidade e desempenho.

Finalidade: Pesquisa

Pesquisador responsável: Sandra Gesteira Coelho

Unidade: Escola de Veterinaria

Departamento: Departamento de Zootecnia

Situação atual: Decisão Final - Aprovado

Aprovado na reunião do dia 25/03/2019. Validade: 25/03/2019 à 24/03/2024

Belo Horizonte, 27/03/2019.

Atenciosamente,

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Universidade Federal de Minas Gerais

CAPÍTULO 2 – ARTIGO CIENTÍFICO

INTERPRETATIVE SUMMARY

Total serum protein and its influence on morbidity, mortality, and performance of pre-weaned dairy calves from different genetic compositions. *Moreira et al.* Heifer rearing represents a large cost for dairy farmers. It is important to understand the risk factors associated with failure of transfer of passive immunity (FTPI) in crossbred calves in tropical conditions, and how it impacts morbidity, mortality, and weight gain during their pre-weaning period. Heterosis, selection for increased milk production, and season of the year affect FTPI, calf morbidity, mortality, and weight gain. We demonstrated that a universal cut-off point for FTPI may not be the most adequate strategy to evaluate FTPI. This may help farmers with their management strategies to maximize animal health and performance.

TOTAL PROTEIN, HEALTH, AND PERFORMANCE OF CROSSBRED DAIRY CALVES

Total serum protein and its influence on morbidity, mortality, and performance of pre-weaned dairy calves from different genetic compositions

Keywords: failure of transfer of passive immunity, neonatal calf diarrhea, bovine respiratory disease, cattle tick fever

ABSTRACT

Heifer rearing represents a large cost for dairy enterprises, but data on risk factors for failure of transfer of passive immunity in tropical countries is scarce. Our objective

was to describe risk factors for failure of transfer of passive immunity (FTPI) and to investigate how FPTI is associated with the risk of morbidity, mortality, and growth of pre-weaned dairy calves from two genetic compositions in tropical conditions. We performed a retrospective cohort study and used pre- and post-birth calf-level data from 6,011 crossbred pre-weaned calves from a single herd, born between 2012-2018. We obtained information on calf pedigree, the season of birth, the occurrence of retained placenta (RP), total serum protein (TSP), morbidity (neonatal calf diarrhea - NCD, bovine respiratory disease - BRD, and tick-borne disease - TBD), mortality, and weight gain. The genetic composition was predominantly dairy Gyr (**PG**, 0-50% Holstein breed), and predominantly Holstein (**PH**, > 50% Holstein breed). Multivariate mixed logistic regression was performed (SAS 9.4). The optimal TSP cut-off points for predicting morbidity and mortality were 7.6 g/L and 6.9 g/L, respectively. The median value of TSP was 7.2 g/L. At cut-off points of 5.2 g/L, 7.6 g/L, and 6.9 g/L the prevalence of FTPI was 2%, 55%, and 31%. PH calves had 1.35 greater odds of having FTPI, and 1.48 greater odds of disease. Calves born from multiparous cows and from calving followed by RP had greater odds of FTPI. Overall, the prevalence of disease was 53%, and 41% of the calves had NCD, 18% had BRD, 10% had TBD. Season, parity order of the dam, sire predicted transmitted ability for mil (PTA milk), and weight at birth were also associated with odds of disease. FTPI was not a good predictor of disease. The overall mortality rate was 6%. Calves PH had 2.99 greater odds of mortality than PG. The mortality risk varied according to an interaction between FTPI and the season of birth, but calves from sires with a positive PTA for milk had greater odds of dying. The average daily gain was 0.636, and calves with FTPI (cut-off point of 5.2 g/L) gained less weight than calves without FTPI. An adequate transfer of passive immunity may not be enough to prevent morbidity and mortality if calves are raised in challenging conditions.

INTRODUCTION

Heifer rearing represents a large cost for dairy enterprises (Santos and Lopes, 2014; Mohd Nor et al., 2015; Overton and Dhuyvetter, 2020). High morbidity, mortality, and low performance during the pre-weaning period increases rearing costs, reduces animal welfare, increases the use of antimicrobials, and negatively impact the performance of the adult cow in the long term (Soberon e Van Amburg, 2013; Shivley et al., 2018b; Laporta et al., 2020). The high morbidity observed is mainly due to neonatal calf diarrhea (**NCD**) and bovine respiratory disease (**BRD**), the most common diseases affecting pre-weaning dairy calves in the U.S. and worldwide (Windeyer et al., 2014; Urie et al., 2018). In the US, previous studies have reported the prevalence of NCD varying from 17% to 23% (Windeyer et al., 2014; Urie et al., 2018), representing 51% of all sick calves (Urie et al., 2018). The prevalence of BRD was reported to vary from 9% to 23% (Windeyer et al., 2014; Urie et al., 2018; Dubrovski et al., 2019), representing 27% of all sick calves (Urie et al., 2018). In tropical conditions, another important disease complex is the tick-borne disease (TBD)). The prevalence of the disease varies between 13% and 65% (Bahia et al., 2020), and the highest incidence happens at approximately 125 days of age (Moreira, 2017; Oliveira Júnior et al., 2018). Calf mortality may vary according to the production system and the breed composition of the herd, with previous studies reporting varying calf pre-weaned mortality rates, from 6% in the US and Canada (USDA, 2018; Winder et al., 2018), to 11% in the Netherlands (Santman Berends et al., 2019). In Brazil, mortality rates are higher, with mortality up to one year of age varying from 8% (Fruscalso et al., 2020) to 17% (IILB, 2019).

The failure of transfer of passive immunity (**FTPI**) is an important factor that negatively affects the health and survivability of dairy calves (Godden, 2008). FTPI is defined as the concentration of serum IgG less than 10 g/L between 24 and 48 hours after birth (Godden et al., 2008; Urie et al., 2018; Lombard et al., 2019). FTPI results in increased morbidity, mortality, and decreased performance up to three months of age, and impaired productive life (Winderyer et al., 2014; Faber et al., 2005: Shivley et. al., 2018a,b). Despite the body of literature supporting the importance of transfer of passive immunity, recent studies reported prevalence of FTPI varying from 11% (Wyndeyer et al., 2014) to 36% (Abuelo et al., 2019) in the United States. In Brazil, recent studies have reported varying prevalence of FTPI, from 16% (Moraes et al., 2000) to 32% (Weiller et al., 2020), and variation in herd size, production systems, management practices, and regions may explain this observed difference.

Data on risk factors for FTPI in tropical countries and its association with pre-weaning dairy calves' morbidity, mortality, and performance is scarce. Therefore, the objectives of this observational study were to describe risk factors for FTPI and to investigate how FPTI is associated with risk of morbidity, mortality, and weight gain of pre-weaned dairy calves from two genetic compositions in a tropical condition. The results of our study are important to the development of strategies to reduce morbidity and mortality in tropical dairy herds.

MATERIAL AND METHODS

This study was approved by the Animal Care Committee of the *Universidade Federal de Minas Gerais* (UFMG), protocol 415/2018.

Dairy Herd and Animal Management

We examined calf data obtained from a dairy farm located in the south part of Minas Gerais state, the largest dairy producer state in Brazil, known for excellent record keeping and for being regularly visited by the first author of this study since the beginning of the data collection period (August 2012). Lactating cows were kept in a semi-confinement system, which consisted of cows grazing on Tifton 85 (*Cynodon spp*) pastures during the rainy season (October to April) and supplemented with corn silage and receiving corn silage exclusively during the dry season (May to September). It was a mixed-breed herd, with most lactating cows being crossbred Holstein (**HO**) - Gyr (**GY**) animals produced by *in-vitro* fertilization and embryo transfer. The lactating herd was composed of 35% cows ½ HO ½ GY, 50% cows ¾ HO ¼ GY, and 15% cows with different breed proportions. Holstein semen was used to produce all embryos. Approximately 5% of the lactating herd was used as donors, and the other cows were used as recipients (dams). The average milk production at 305 days was 5,800 kg. During the data collection period, the average number of lactating cows/day varied from 1,024 (2012) to 1,728 (2018). Cows were dried-off 90 days before the expected calving date, and dry cows were kept in dry-lots. Thirty days before calving, dry cows were transferred to maternity pens, which consisted of five areas with shade, covered with Tifton 85 grass (rotated weekly), and a work area used for calving assistance and calf management. Dry cow diets consisted of corn silage, soybean meal, and mineral supplementation. No DCAD diet was supplemented to the cows during the prepartum period.

All calvings that happened from 4 am to 8 pm were watched by trained personnel, and calves received an average of four liters of colostrum between 1 and 6 hours after birth. The dam's colostrum was harvested and evaluated for quality, and if the BRIX was equal to or greater than 23%, her colostrum was used. If not, colostrum from the colostrum bank was used instead. Calvings that happened between 8 pm and 4 am were not watched, and calves received colostrum following the described protocol at 4 am, after the employee's arrival. Navel dip was performed after birth (day calvings) or after employee arrival (night calvings) with a 10% iodine solution, and twice daily for 5 days afterward. Calves were weighted by using an adapted scale (PR5CL-200, Precision, Tupã, Brazil), right after birth or after the arrival of the morning employee.

The calves were separated from their dams 12 hours after birth, approximately. Calves were raised individually, in a tropical system (Figure 1). The area consisted of rows of calves 3.5 meters apart from each other, in an area covered with Tifton 85 (*Cynodon* spp). Each calf received a leather collar and a 1.5-meter chain, attached to an 8.5-meter steel wire. Water and milk buckets were located at one end of the wire. This system allowed calves access to water and concentrate, as well as forage consumption. Halfway to the length of the wire, a shaded area was provided (4.5 m^2 (3,0 m x 1,5 m)), with an additional automatic water drinker.

All calves received transition milk for up to three days of age. After this period, calves received pasteurized waste milk and milk replacer (*Sprayfo Violeta*, 20% protein, 16% fat, 46% lactose, and 4,178 kcal/kg metabolized energy, Sloten, Netherlands). Milk replacer was used only when the volume of waste milk was not enough to feed all calves (dry season). Older calves were prioritized to received milk replacer. The objective of the farm was to keep calves receiving a liquid diet for at least 70 days; however, a minority of calves received a liquid diet for a shorter period due to calf facility constraints. Milk was offered in a bucket with a teat, and calves received six liters of milk from 1 to 35 days of age twice daily, followed by 3 liters once a day until weaning. Water and concentrate (22.15% protein, 0.86 Mcal of energy/kg dry matter) were provided *at libitum* since day two of life. Throughout the pre-weaning period, calves were visually evaluated daily by trained farm personnel. After weaning, calves were kept in the same installation for seven days, receiving the transition diet.

Study Design

Individual Calf Data. This study is a retrospective cohort study. We obtained pre- and post-birth calf-level data from the farm's management software IDEAGRI®, from calves born alive between August 9th, 2012 and August 8th, 2018 (n=9,966). The dataset contained information on the breeding date that resulted in conception, embryo transfer date, breeding type (natural service, artificial insemination, or embryo transfer), parity order of the dam (first, second, and third plus parities), donor and sire identification, retained placenta at calving, and dam's weight at calving. Additionally, the dataset contained each calf's date of birth, birth weight, genetic composition, total serum protein (**TSP**), cases of disease (NCD, BRD, and TBD events) and their dates, weaning date, and weaning weight.

From the data above, we identified the calf season of conception and season of birth. Farm weather data was obtained from the *Usina Hidreletrica de Furnas*, located 15 km from the farm (Figure 2). We used the astronomical definition of the season because it better reflects the raining pattern of the region (NOAA, 2019). Summer was from December to February, fall was from March to May, winter was from June to August, and spring was from September to November. Gestation length was calculated by subtracting the date of conception from the date of birth (for calves produced by artificial insemination, and additional 7 days were subtracted to account for the date of transferring for calves produced by embryo transfer). The pre-weaning period was determined by subtracting the date of birth from the weaning date. The total weight gain was calculated by subtracting the birth weight from the weaning weight, and average daily gain during the pre-weaning period was calculated by dividing the total weight gain by the pre-weaning period (in days).

Disease and Mortality Records. At 6 am daily, the fecal and respiratory scores of all calves were visually evaluated by trained farm personnel. Farm employees were routinely trained by the first author of this study. For the diagnostic of NCD and BRD, the employees were trained according to the methodology proposed by McGuirk (2008). Briefly, fecal scores were graded as follows: 0 – normal (firm but not hard); 1 – soft (does not hold form, piles but spreads slightly); 2 – runny (spreads readily to about 6 mm depth);

and 3 – watery (liquid consistency, splatters). Respiratory score evaluations were adapted from McGuirk (2008). Rectal temperature was classified as 0 – temperature between 37.8 and 38.3 ºC, 1 – temperature between 38.4 and 38.8 ºC, 2 – temperature between 38,9 and 39.3 ºC, 3 – temperature above 39.4 ºC. Cough scores were 0 – none, 1 – induced single cough, 2 – induced repeated or occasional spontaneous coughs, 3 – repeated spontaneous coughs. Nose score was 0 – normal serous discharge, 1 – small amount of unilateral cloudy discharge, 2 – bilateral cloudy or excessive mucus discharge, 3 – copious bilateral mucopurulent discharge. Eye scores were 0 – normal, no discharge, 1 – a small amount of ocular discharge, 2 – moderate amount of bilateral discharge, 3 – heavy ocular discharge. Lastly, ear scores were 0 –normal, 1 – ear flick or head shake, 2 – slight unilateral drop, 3 – head tilt or bilateral drop. If the calf presented with two or more of any of the described signals, she would receive treatment. The diagnostic of TBD was given if calves were apathetic, with increased heart and respiratory rates, pyrexia, weakness, lethargy, anorexia, and presented pale mucosa (Kocan et al., 2010). Cases of the same disease were considered independent if at least14-days apart. Other diseases were not recorded as they were not part of the calf health management program of the farm. All diagnoses, treatments, and mortality were recorded in an individual calf card and daily transferred to the management software system by a trained employee. The age at the disease event was calculated by subtracting the date of birth from the date recorded for the disease event, and it was divided into three periods: from birth to 14 days, from 15-35 days, and from 36 to weaning.

Sire Information. We obtained each calf's sire predicted transmitting ability for milk (**PTA milk**) and net merit **($NM)** genetic information from *"The Council of Dairy Cattle Breeding*" (CDCB, 2019). We grouped the calves according to their sire PTA milk and $NM as positive (values equal or greater than 0), or negative (values lower than 0).

Data Management

Initially, our dataset contained records from 9,966 calves. We checked the dataset for inconsistencies in each calf record. We excluded records from calves born from artificial insemination (1,112), natural service (261), and 100% Holstein (115) as they were concentrated in three years only (all born from 2012 to 2015) or did not have the date of breeding. Therefore, all calves left in our dataset were produced by *in vitro* embryo transfer. We excluded data from calves with a pre-weaning period less than 50 and greater than 120 days (7). Additionally, we excluded 13 calves that had a weaning date but no other information during the pre-weaning period. We excluded 1,961 calves without TSP information, and 132 with TSP > 10 g/L. We excluded additional records without sire PTA milk and $NM information (198), with gestation length less than 260 days or greater than 300 days (51), and without the parity order of dam (105). The remaining calves in our dataset (6,011) were divided into two groups, according to breed composition: predominantly dairy Gyr (**PG**, 0 to 50% Holstein breed), and predominantly Holstein (**PH**, more than 50% of Holstein breed).

Total Serum Protein and Failure of Transfer of Passive Immunity

Whole blood samples were taken from the auricular artery 24 to 48 hours after colostrum intake by a trained employee (sterile blood collection tube without anticoagulant, Perfecta, São Paulo, Brazil). The samples were centrifuged at 3,000 rpm for 10 minutes (20 a 24 °C) (SPIN 1000, Microspin, Jacareí, Brazil). Total serum protein was evaluated by using a refractometer (RHS-28ATC, SC Metra s.r.l., Oradea, Romania).

We used the methodology proposed by Windeyer et al. (2014) to calculate the sensitivity and specificity for predicting disease (NCD, BRD, or TBD) and mortality, using different TSP cut-points. Briefly, sensitivity and specificity for morbidity and mortality were calculated for TSP cut-off points varying from 4,2 to 7,8 g/L, with increases of 0.1 g/L. The sum of sensitivity and specificity at equal weight for each cut-off point is the most appropriate approach to minimize both false positives and false negatives (Windeyer et al., 2014). Therefore, the TSP cut-off point with the highest sum was defined as the threshold to define failure of TSP or not in the regression analyses. The objective was to truly detect animals at risk for disease and mortality, but also to avoid overestimation of FTPI. Additionally, we calculated the positive and negative predicted values for each cut-off point.

Statistical Analyses

We calculated the incidence rate of NCD, BRD, and TBD for calves up to weaning by dividing the number of first cases of diseases observed from birth to weaning by the total number of calves born (at risk). Additionally, we calculated the incidence rate for each disease according to age group interval (1 to 14 days; 15 to 35 days; 36 to weaning) by dividing the number of calves with disease reported in the age period by the number of calves at risk in that period. The population attributable fraction (the proportion of disease in the population that is attributable to FTPI) was calculated by subtracting the morbidity in the group without FTPI from the overall morbidity and dividing it by the overall morbidity (Dohoo et al., 2014). The mortality rate and attributable fraction for mortality were calculated similarly.

All analyzes were performed in SAS 9.4. All independent continuous variables were evaluated for normality and multicollinearity by using PROC UNIVARIATE and PROC CORR. Descriptive data were analyzed by using PROC FREQ and PROC MEANS (for categorical and continuous variables, respectively). Time in days to disease event or mortality were analyzed by using Cox proportional hazard (PROC PHREG and LIFETEST, SAS 9.4), and the STRATA statement was used to visualize differences according to FTPI at the threshold of 5.2 g/L. Multivariate analyzes were conducted by using PROC MIXED and PROC GLIMMIX (SAS 9.4), with the year of birth as a random variable to account for clustering of calves within a year of birth, following the approach described below.

Multi-level logistic and linear regression models were constructed to determine the factors associated with the odds of FTPI, morbidity, mortality, and average daily weight gain during the pre-weaning period. The independent variables for each model were chosen according to their potential biological effect on the response being studied. Only calves with full data were included in the analyses. A three-step approach was used to select the variables to be included in the final multivariate model. First, univariate analyses for each independent variable were performed with the year as a random effect, and variables were ranked according to their P-value. Second, multivariate analyses were performed by using PROC MIXED and GLIMMIX with maximum likelihood and Laplace parameter estimation methods, respectively. All variables were offered to the model according to their P-value from the univariate analysis (smallest to largest), and the model *Akaike Information Criteria* (AIC) was used to select the final model variables (stepwise elimination approach). The model with the lowest AIC was used. Finally, PROC MIXED and GLIMMIX were used with REML and RSPL default specifications for parameter estimation, first-order interactions for all variables were added to the model, and significant ones were kept. For the analysis of mortality and daily weight gain, two models were used, one with data from all calves, the other with data from only calves with disease. Only calves surviving to wean were included in the analysis of daily weight gain, and different thresholds for TSP were tested for significance as well.

RESULTS

Table 1 summarizes the descriptive values of calf raising in the farm of this study. In our final dataset, 34.6% (2,078) of all calves were PG, and 65,4% (3,933) were PH, all born from in vitro fertilization and embryo transfer. Thirty-seven percent of all calvings happened in the fall, followed by 24% in the winter, 23% in the summer, and 16% in the spring. The median age at weaning was 80 days (range: 50-120), with variation according to the season of birth. Calves born during winter and spring were weaned later (median of 88 and 85 days) than calves born during summer and fall (median of 75 and 77 days). The incidence of retained placenta was greater following the birth of PH calves (12%) compared to PG births (8%, $P < 0.0001$), but no differences due to season of calving were observed ($P = 0.2025$).

Failure of Transfer of Passive Immunity

The median value of TSP was 7.2 g/L (range: 4.0 – 9.9, Table 1). Using the cut-off point of 5.2 g/L, the prevalence of FTPI was 2% (111 calves out of 6,011). The optimal cut-off point for predicting morbidity during the pre-weaning period was 7.6g/L (sensitivity: 57%, specificity: 46%). For this cut-off value, the positive predicted value (**PPV**) and negative predicted value (**NPV**) were 55% and 49%, respectively. The prevalence of FTPI when the cut-off point of 7.6 was used was 55% (3,352 calves out of 6,011). To predict mortality, the optimal cut-off value was 6.9 g/L (sensitivity: 39%, specificity: 69%, PPV: 7%, NPV: 95%). Using the cut-off point of 6.9 g/L, the prevalence of FTPI was 31% (1,881 calves out of 6,011 calves).

Using the optimal cut-off point of 7.6 g/L, the attributable fraction for disease during the pre-weaning period due to FTPI was 3.8%. Specifically, for NCD, BRD, and TBD attributable fractions were, 6.3%, 3.7%, and 0.3% respectively. For mortality, the attributable fraction was 2.2% for the threshold of 6.9 g/L.

The risk factors for FTPI (at the cut-off of 7.6 g/L) are shown in Table 2. PH calves had greater odds of having FTPI (OR: 1.35, CI: 1.20 – 1.52) than PG calves. Calves born from multiparous cows (second and third plus lactations) had greater odds of FTPI (1.15, CI: 1.01 – 1.32, and 1.24, CI 1.09 – 1.41, respectively), and this was independent of the retained placenta status, with calves born from calving followed by a retained placenta event having greater odds of FTPI (OR: 1.24, CI 1.04 – 1.47) than calves born from calvings without this occurrence.

Morbidity

The prevalence of disease was 53%, i.e., 3,192 calves (out of 6,011) had at least one case of disease reported. Over 41% of the calves had NCD (2,496 calves), 18% had BRD (1,090 calves), and 10% had TBD (572) (Table 1). Among the animals who had a disease event, 65% had only one case reported (2,060), 25% had two cases reported (809), and 10% (323) had three or more cases reported. The disease incidence rate was greater in the period from birth to 14 days (72%, 2,310 calves out of 3,192), followed by the period from 15-35 days (18%, 584 calves), with 9% of all disease happening from 36 days to weaning (298 calves). The median age at the first disease case was 11 days, with the median age of the first case of NCD, BRD, and TBD being 11, 15, and 37 days, respectively.

The risk factors for morbidity are presented in Table 3. Calves born in the winter (OR: 1.66, CI 1.41-1.95), fall (OR: 1.56, CI: 1.35-1.80), and spring (OR: 1.34, CI: 1.12 – 1.6) had greater odds of disease when compared to calves born in the summer. Calves born from second (OR: 1.24, CI: 1.8-1.42) and third (OR: 1.23, CI: 1.08-1.40) parity dams had greater odds of disease when compared to calves born from primiparous dams. Calves from sires with a positive PTA milk had greater odds of disease (PR: 1.16, CI 1.01 – 1.34) than calves whose sires had a negative PTA milk. Calves PH had greater odds of disease when compared to PG calves (OR: 1.48, CI: 1.31 – 1.66). The weight at birth was also significantly associated with the odds of disease, and every additional kg at birth compared to the overall average (36 kg) meaning lower odds of disease (OR: 0.982, CI:

9.973-0.992). Having a case of diarrhea was significantly associated with greater odds of BRD (OR: 1.56, CI: 1.36-1.79) and TBD (OR: 1.93, CI: 1.61 – 2.32) (results not shown). Kaplan-Meier survival curves for the non-disease probability for calves with FTPI (thresholds of TSP < 5.2g/L and < 7.6 g/L) and without (TSP ≥ 5.2 g/L and ≥ 7.6g/L) are presented in Figure 3. When we used the 5.2 g/L cut-off for FTPI, breed composition (P = 0.0009), season of birth (P = 0.0220), and an interaction between these two factors (P = 0.0030) were significantly associated with time to disease. Although not significant, there was a tendency (P=0.0614) for interaction between breed composition and FTPI (Figure 3a). When the TSP cut-off of 7.6 g/L was used, breed composition (P < 0.0001), the season of birth (P = 0.0221), and interaction between breed composition and season of birth were significant (P = 0.0035) (Figure 3b).

Mortality

The overall mortality rate was 6% during the pre-weaning period (355 calves died out of 6,011). The median number of days at death during the pre-weaning period was 17. The mortality rate was greater from 1 to 14 days, and between 15 to 35 days of age (41% and 40%, respectively). NCD was responsible for 41% of all mortality cases (145 calves), followed by BRD (21%, 76 calves) and TBD (7%, 25 calves).

The risk factors for mortality are presented in Table 4. Calves PH had greater odds of mortality than PG calves (OR: 2.99, CI: 2.24 – 4.01). Calves from sires with a positive PTA milk had greater odds of dying (OR: 1.48, CI: 1.06-2.05). There was an interaction between FTPI and the season of birth. Calves without FTPI born in the winter (OR: 0.40, P = 0.0007), spring (OR: 0.43, P = 0.0193), and fall (OR: 0.59, P = 0.0418) had lower odds of mortality than calves born in the summer; however, no differences due to season were observed in calves with FTPI. Among the calves who had at least one case of disease, PH calves (OR: 1.75, CI 1.15-2.67), calves from sires with positive PTA milk

(OR: 1.96, CI: 1.09-3.52), and an increase in the average age at the first case of disease (OR from 16 to 17: 0.98, CI: 0.96-0.99) were significantly associated with the odds of mortality during the pre-weaning period (data not shown). Kaplan-Meier survival curves for the survival probability for calves with FTPI (TSP < 5.2g/L) and without (TSP ≥ 5.2 g/L) are presented in Figure 4. When the threshold of 5.2 was used to define FTPI, breed composition (P < 0.0001), parity order of the dam, (P = 0.0191), and FTPI (threshold 5.2 g/L, P < 0.0001) were significantly associated with time to mortality. There was a tendency (P = 0.0529) for the interaction between the season of birth and parity order of the dam. When the threshold of 6.9 g/L was used, breed composition (P < 0.0001), parity order of the dam, (P = 0.0399), and FTPI (threshold 6.9 g/L, P < 0.0011) were significantly associated with time to mortality, and a tendency was observed for the interaction of season of birth and parity order of the dam (P = 0.0897).

Daily Weight Gain During the Pre-weaning Period

The results for the average daily gain model are shown in Table 5. For this analysis, 5,333 calves were used. Overall, the average (std) daily gain was 0.636 (0.129) kg. Calves with FTPI at the cut-off point of 5.2 g/L gained less weight than calves without FTPI (0.627 versus 0.660 kg/day, respectively, P=0.0122). There was an interaction between season of birth and breed composition, weight at birth, gestation length, case of disease, and parity order of the dam. Also, an interaction between the sire PTA milk and having a case of disease was observed. The PG calves had a greater average daily gain than PH calves, but the largest difference was observed for calves born in the summer (difference of 0.051 grams, P<0.0001). For the same weight at birth, calves born in the fall and winter gained 0.006 and 0.003 kg/day compared to calves born in the summer or spring (P<0.0001), and for the same gestation length, calves born in the fall and winter gained less 0.003 and 0.002 kg/day than calves born in the summer or spring (P<0.0001). Calves without disease had a greater weight gain than calves with at least one occurrence of disease, but the difference varied according to the season of the year, and the largest difference was observed for calves born in the winter (0.047 kg/day, P<0.0001). There was an interaction between sire PTA milk and having a case of disease. Calves who had one case of disease had a lower average daily gain than calves without disease, but the difference was larger for calves born from sires with positive PTA milk (0.049, P<0.0001). Calves born from first parity dams gained overall less weight per day than calves born from second and third parity order dams; however, the difference was larger for calves born in the summer (the difference between second and third versus first parity: 0.043 and 0.030 kg/day, respectively) and spring (the difference between second and third versus first parity: 0.053 and 0.033 kg/day, respectively). Also, for calves without FTPI (cut-off point of 5.2 g/L), no differences were observed in their average daily gain regarding their sire PTA milk, but calves with FTPI from sires with positive PTA milk gained less weight (0.6213 kg/day) than calves from sires with a negative PTA milk (0.6433 kg/day, P=0.0106).

When only calves with a case of disease were compared, calves that had TBD gained less weight than calves with BRD and NCD (0.611, 0.632, and 0.667, respectively, P < 0.0001, results not shown). Calves from sires with positive PTA milk had a lower average daily gain (0.625) than calves from sires with negative PTA milk (0.648, P < 0.0001). There was an interaction between season of birth and gestation length, weight at birth, breed composition, and dam's parity order. For the same gestation length, calves born in the fall with at least one case of disease gained 0.002 kg/day less (P = 0.0002), and for the same weight at birth, also calves born in the fall gained 0.005 kg/day more compared to calves born in in the other seasons (P < 0.0001). PH calves gained 0.043 kg/day less than PG calves in the summer, and PG calves gained more weight in the summer (0.667 kg/day) when compared to PG calves born in the winter (0.627), fall

(0.636), and spring (0.625) (P<0.0001). Calves from third parity dams gained more weight than calves from first parity dams in the summer (0.654 versus 0.620, P = 0.0020).

DISCUSSION

Risk factors for FTPI are well documented in the literature, however, risk factors for FTPI under tropical conditions and crossbred calves are not well described. In the present cohort study, we described the risk factors for FTPI, and how it impacts morbidity, mortality, and daily weight gain in pre-weaning dairy calves from two genetic compositions in a tropical condition.

Overall, the values for TSP observed in our study were higher than others reported in the literature, with similar ranges (Winderyer et al., 2014; Tyler et al., 1996; Trotz-Williams et al., 2008). Traditionally, a cut-off value of 5.2 g/L for TSP and 10 g/L for serum concentration of IgG has been used as a threshold for FTPI (Calloway et al., 2002). New thresholds for IgG have been proposed to improve sensitivity, specificity, PPV, and NPV to predict morbidity. Recent publications have suggested an increase in the cut-off point for the serum concentration of IgG in neonatal calves, with new thresholds varying from 15 g/L to 25 g/L, and TSP varying from 5.8 g/L to 6.3 g/L (Furman-Fratczak et al., 2011; Chigerwe1 et al., 2015; Urie et al., 2018). For instance, the best TSP cut-off point found by Windeyer et al. (2014) to predict BRD was 5.7 g/L; however, they used data from multiple farms in Canada and Minnesota, and the median TSP in their study was 6.0 g/L (range 3.6 – 10).

Crossbred ½ HO ½ Gyr cows produce colostrum with a higher concentration of immunoglobulins than Holstein cows (Soares Filho et al., 2001). Quigley (2001) suggested the use of an equation to calculate the volume of colostrum intake necessary to achieve a minimum required plasma concentration of IgG of 10 g/L. Brix and IgG concentration have a correlation coefficient of 0.75, thus colostrum with 23% Brix would mean 68 g/L of IgG in the colostrum. Assuming calves were fed 4 liters of colostrum with a Brix concentration above 23%, an average calf weight of 35.5 kg, 9% of body weight of plasma volume (3.2 liters), and apparent efficiency of absorption of 35%, calves on the farm where data for this study was obtained would require an IgG intake of 91.4 grams of IgG. This would require a volume of 1.4 liters of colostrum, much below the default amount provided to the calves of this study. Also, the improvement of colostrum management in this specific farm has been an objective since 2008. Employee training has been reported as positively impacting colostrum management in dairy herds (Ramirez et al., 2017; Hesse et al., 2019).

Breed and parity order influenced FTPI in the present study. These two factors have been reported as influencing colostrum composition and quality (Weaver et al., 2000; Zarcula et al, 2010; Conneely et al., 2013), although contrasting results in the literature about the effect of parity in the colostrum quality of crossbred cows exist (Tyler et al., 1999; Coleman et al., 2015). Besides, the average age at first calving on our dataset was 30 months, compared to 24 months on average of Holstein cows in the US. In our study, PG calves had lower odds of FTPI. Differences in immunoglobulin absorption and TSP due to breed have been reported for Jersey versus Holstein calves (Jones et al., 2004), and for Jersey X Holstein crossbred versus Holstein calves (Maltecca et al., 2006), with the transfer of passive immunity described to be more effective in Jerseys and crossbred calves. PG calves on the farm of this study were the F1 generation, and heterosis may play a role in the absorption of immunoglobulins. Breeding programs, including crossbreeding, have been proposed as an alternative to enhance disease resistance (Begley et al., 2009), and deserve further investigation. Calves from births followed by a retained placenta occurrence had increased odds of FTPI. We did not have information on which calvings needed assistance but retained placenta occurrences are known to be more frequent in calvings with obstetrical assistance (Kovacs et al., 2016). FTPI may happen after a difficult birth due to respiratory acidosis, reduced suckling ability, and impaired absorption of immunoglobulins (Renaud et al., 2020).

Despite the high values of TSP reported, the incidence of disease was high, and similarly to other studies, NCD and BRD were the most common diseases observed (Urie et al., 2018). The incidence of NCD was higher than the values of 18% and 21% reported by Windeyer et al. (2014), Urie et al. (2018), and Abuelo et al. (2019). However, incidences as high as 37% and 50% of NCD have also been reported in the literature (Furman-Fratczak et al., 2011; Lora et al., 2018). Incidence of BRD was also high when compared to values of 6% and 9% reported by Abuelo et al. (2019) and Urie et al. (2018), but variation among herds exists (Windeyer et al., 2014; Karle et al., 2019). Heterosis favors health and longevity characteristics (Bunning et al., 2019), and there are heterosis losses when F2 are compared to F1 generations (Willham e Pollak, 1985). In our study, PG calves had lower odds of disease. PG calves were the first generation (F1) of the cross between cows GL and Holstein sires, and calves PH (F2) were the second generation of the crossing of cows ½ HO ½ GL and Holstein sires. Besides, for many years, the selection objective has focused on improvements of production and type characteristics, which resulted in an indirect selection for impaired health (Miglior et al., 2017). This is in accordance with our findings that calves from sires with a negative PTA milk had lower odds of disease than calves from sires with a positive PTA milk. Season of the year influenced the incidence of disease, likely due to a greater variation in the daily temperature during fall and spring months in the region studied (Figure 2; Urie et al., 2018). Also, these calves are exposed to an infestation of ticks and flies during the summer, which may help to explain the greater incidence of disease and mortality during this season.

Although FTPI has been reported as a risk factor for NCD (Raboisson et al., 2016; Lora et al., 2018), in our study it was not a good predictor for morbidity, in agreement with Windeyer et al. (2014). Previous studies have demonstrated that passive immunity may be protective against diarrhea caused by rotavirus (Kohara and Tsunemitsu, 2000), but it is still unclear its effect against Cryptosporidium spp. (Trotz-Williams et al., 2008; Lora et al., 2018). Therefore, the role of TSP on the occurrence of NCD according to the causal agent deserves further investigation. The overall mortality risk was similar to others reported elsewhere in the world and following the higher incidence of NCD (Lora et al., 2018). FTPI was associated with higher mortality (Windeyer et al., 2014; Lora et al., 2018), with higher rates observed during summer.

The average daily gain of the calves was similar to others reported in the literature (Virtala et al., 1996; Bateman II et al., 2012), but less than the 0.950 kg/day reported by Windeyer et al. (2014). The season of birth had an important effect on the average daily gain. The farm rearing system does not control for thermal stress, with calves being exposed to a high amplitude of temperature during fall and spring. During summer, despite the higher incidences of disease and mortality, overall calves had a greater average daily weight gain. On this farm, during summer calves had a greater supply of waste milk due to a higher incidence of mastitis in the study herd, and therefore milk replacer represented a minor part of their liquid diet (Godden et al., 2005)). Among calves who had at least one case of disease, the greatest weight gain was observed in calves with NCD. NCD cases occurred at a median of 11 days. At this age, the main source of nutrients supply for the calf was milk or milk replacer, and 6 liters/day were provided to all calves. Therefore, the nutritional requirements for an average calf weighing 40 kg were being supplied at 257% or 198%, respectively (NRC, 2001), even if a decrease in consumption was observed. This may also explain why heavier calves gained less weight when sick, as the supply of nutrients per kilo of body weight was slightly less when compared to smaller calves (NRC, 2001). Furthermore, among the three diseases studied, diarrhea is the most obvious and with the easiest diagnosis. The early identification of the disease and treatment may have favored the weight gain of animals identified with diarrhea.

Our study was a retrospective cohort study using data from one farm in Brazil known for excellent personal training and health record-keeping overseen by the first author of this study. Despite the importance of the results here presented, this study is not a random sample of the target population, and extrapolation of results should be done with caution. Due to the long-term technical relationship and work developed on the herd where this study was conducted, it may likely be better managed than other herds in the same region. Nonetheless, this herd represents the most common dairy system in Brazil, and thus this study provides valuable information on the management of dairy calves from two different genetic compositions raised under tropical conditions.

Our results indicate that an adequate transfer of passive immunity may not be enough to prevent morbidity and mortality if calves are raised in challenging conditions such as extreme weather and in an environment with high pathogen pressure. It demonstrates that a universal cut-off point may not be the most adequate strategy for evaluating FTIP, and each farm should have a unique threshold based on their rearing systems characteristics and challenges.

CONCLUSIONS

Selecting for increased production may affect the ability of calves to respond to challenges during the rearing period. FTPI was a poor predictor of morbidity and mortality, even when higher cut-off values of TSP of 7.6 g/L and 6.9 g/L (respectively) were used. An adequate transfer of passive immunity may not be enough to prevent morbidity and mortality if rearing conditions are challenging. It demonstrates that a universal cut-off point may not be the most adequate strategy for evaluating FTIP, and each farm should have a unique threshold based on their rearing systems characteristics and challenges.

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Table 1. Descriptive statistics for pre-weaning calves raised in a dairy farm in southeast Brazil

	Median (min-max)		
	Overall	Breed composition[1]	
		PH	PG
N	6,011	3,933	2,078
Average days at weaning	80 (50-120)	80 (50-120)	81 (55-119)
Spring	85 (52-116)	84 (52-116)	85 (57-114)
Winter	88 (58-120)	87 (59-120)	90 (50-119)
Fall	77 (52-118)	77 (52-118)	77 (58-118)
Summer	75 (50-117)	73 (50-117)	78 (55-117)
Gestation length (days)	278 (260-300)	277 (260-299)	279 (260-300)
Weight at birth (kg)	35 (23-55)	36 (23-55)	35 (23-55)
Weight at weaning (kg)	86 (50-192)	85 (50-163)	87 (5-192)
Incidence of retained placenta (%)	10.5 (-)	12.0 (-)	7.6 (-)
Age at first case of disease (days)	11 (1-108)	11 (1-100)	11 (1-108)
NCD[2]	11 (1-83)	10 (1-74)	11 (1-83)
BRD[3]	15 (1-97)	15 (1-97)	16 (1-92)
TBD[4]	37 (1-108)	35 (1-100)	41 (1-108)
Incidence of disease (%)	53.1 (-)	56.9 (-)	45.7 (-)
NCD	41.5	45.2	34.5
BRD	18.1	19.9	14.9
TBD	9.5	10.1	8.4
Mortality (%)	5.9	7.5	3.0

[1]PH: predominantly Holstein, PG: predominantly dairy Gyr.
[2]NCD: Neonatal calf diarrhea
[3]BRD: Bovine respiratory disease
[4]TBD: Tick-borne disease

Table 2. Multi-level logistic regression model of risk factors associated with failure of transfer of passive immunity (FTPI[1]) in 6,011 calves from a dairy farm in southeast Brazil

Variable	Estimate	SEM	P-value	OR (95% CI)
Intercept	0.079	0.026	0.7709	
Season of birth			0.0269	
Spring	-0.084	0.093		0.919 (0.766-1.103)
Winter	0.144	0.082		1.155 (0.984-1.357)
Fall	-0.055	0.072		0.946 (0.821-1.091)
Summer	*Reference*			
Breed composition[2]			< 0.0001	
PH	0.301	0.059		1.351 (1.203-1.517)
PG	*Reference*			
Dam's parity			0.0034	
1	*Reference*			
2	0.140	0.068		1.151 (1.007-1.315)
3	0.216	0.065		1.242 (1.093-1.410)
Retained placenta at birth			0.0188	
Yes	0.211	0.089		1.235 (1.036-1.472)
No	*Reference*			

[1]Calves were classified as FTPI if the total serum protein was below 7.6 g/L.
[2]PH: predominantly Holstein, PG: predominantly dairy Gir.

Table 3. Multi-level logistic regression model of risk factors associated with morbidity during the pre-weaning period of dairy calves from a dairy farm in southeast Brazil

Variable	Estimate	SEM	P-value	OR (95% CI)
Intercept	-0.074	0.271	0.7952	
Season of birth			< 0.0001	
Spring	0.293	0.093		1.340 (1.117-1.608)
Winter	0.507	0.082		1.660 (1.413-1.950)
Fall	0.444	0.073		1.559 (1.351-1.799)
Summer	*reference*			
Breed composition[2]			< 0.0001	
PH	0.392	0.059		1.480 (1.317-1.664)
PG	*Reference*			
Dam's parity			0.0015	
1	*Reference*			
2	0.213	0.068		1.238 (1.082-1.417)
3	0.204	0.066		1.227 (1.078-1.396)
Sire PTA milk			0.0408	
Positive	0.149	0.072		1.161 (1.006-1.339)
Negative	*reference*			
Weight at birth[3]	-0.018	0.005	0.0002	0.982 (0.973-0.992)

[1]Calves were classified as FTPI if the total serum protein was below 7.6 g/L.
[2]PH: predominantly Holstein, PG: predominantly dairy Gir.
[3]Odds ratio for calves born one kg heavier than the average weight at birth (35.9 kg).

Table 4. Multi-level logistic regression model of risk factors associated with mortality during the pre-weaning period of dairy calves from a dairy farm in southeast Brazil

Variable	Estimate	SEM	P-value	OR (95% CI)
Intercept	-3.596	0.297		
Season of birth			0.0807	
Spring	-0.853	0.256		0.818 (0.546-1.224)
Winter	-0.920	0.219		0.640 (0.452-0.908)
Fall	-0.527	0.171		0.878 (0.652-1.183)
Summer	*Reference*			
Breed composition[1]			< 0.0001	
PH	1.098	0.148		2.997 (2.242-4.007)
PG	*Reference*			
Sire PTA milk			0.0194	
Positive	0.391	0.167		1.478 (1.065-2.050)
Negative	*Reference*			
FTPI[2]			0.0008	
Positive	-0.335	0.237		1.478 (1.065-2.050)
Negative	*Reference*			
Interaction between season of birth and FTPI			0.0031	

[1]PH: predominantly Holstein, PG: predominantly dairy Gir.
[2]Calves were classified as FTPI if the total serum protein was below 6.9 g/L.

Table 5. Multi-level logistic regression model of risk factors associated with average daily weight gain (kg) during the pre-weaning period of dairy calves from a dairy farm in southeast Brazil

Variable	Estimate	SEM	P-value	LS Means (kg/day)
Intercept	-0.529	0.187	0.0311	
Season of birth			0.0023	
Spring	-0.201	0.288		0.641
Winter	0.482	0.250		0.654
Fall	0.647	0.234		0.628
Summer	*Reference*			0.650
Breed composition[1]			0.0094	
PH	-0.051	0.007		0.639
PG	*Reference*			0.648
Dam's parity			<0.0001	
1	*Reference*			0.630
2	0.043	0.009		0.651
3	0.030	0.008		0.650
Sire PTA milk			0.0090	
Positive	-0.0004	0.006		0.634
Negative	*Reference*			0.649
Case of disease[2]			<0.0001	
Yes	-0.001	0.010		0.632
No	*Reference*			0.654
FTPI[3]				
Yes	-0.033	0.013	0.0122	0.627
No	*Reference*			0.660
Weight at birth	-0.008	0.0006	<0.0001	-
Gestation length	0.006	0.0007	<0.0001	-
Interaction: season of birth and breed composition			<0.0001	
PH*winter	0.051	0.010		0.654
PH*fall	0.052	0.009		0.628
PH*spring	0.063	0.011		0.646
PH*summer	0			0.625
PG*winter	0			0.654
PG*fall	0			0.627
PG*spring	0			0.635
PG*summer	0			0.676
Interaction: season of birth and case of disease			<0.0001	
Winter*disease yes	-0.037	0009		0.630
Winter* disease no	0			0.679
Fall* disease yes	0.009	0.009		0.626
Fall* disease no	0			0.629
Spring* disease yes	-0.013	0.010		0.628
Spring* disease no	0			0.653
Summer* disease yes	0			0.645
Summer* disease no	0			0.656
Interaction: season of birth and dam's parity			<0.0001	
Winter*1	0			0.656
Winter*2	-0.56	0.011		0.643
Winter*3	-0.024	0.011		0.663
Fall*1	0			0.624
Fall*2	-0.038	0.010		0.629
Fall*3	-0.024	0.010		0.630

Spring*1	0			0.612
Spring*2	0.010	0.013		0.665
Spring*3	0.003	0.012		0.645
Summer*1	0			0.626
Summer*2	0			0.669
Summer*3	0			0.654
Interaction: sire PTA milk and case of disease			0.0106	
Positive*yes	-0.215	0.008		0.621
Positive*no	0			0.654
Negative*yes	0			0.643
Negative*no	0			0.654
Season of birth and gestation length			<0.0001	
Season of birth and weight at birth			<0.0001	

[1]PH: predominantly Holstein, PG: predominantly dairy Gyr.
[2]Calves that had at least one case of disease
[3]Calves were classified as FTPI if the total serum protein was below 5.2 g/L.

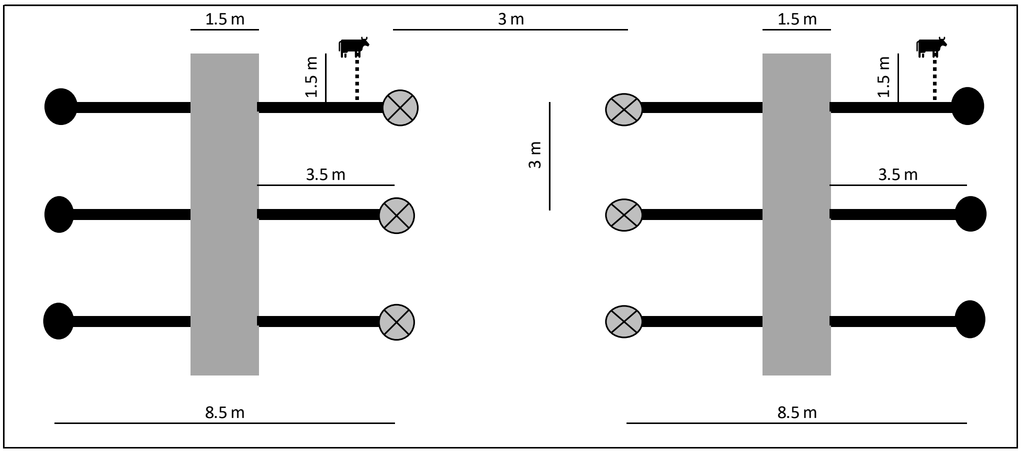


Figure 1. Rearing facilities at the farm. The gray area represents the shade available for calves. Black dots represent where the calves received their milk (buckets with teat), gray dots represent buckets for grain.

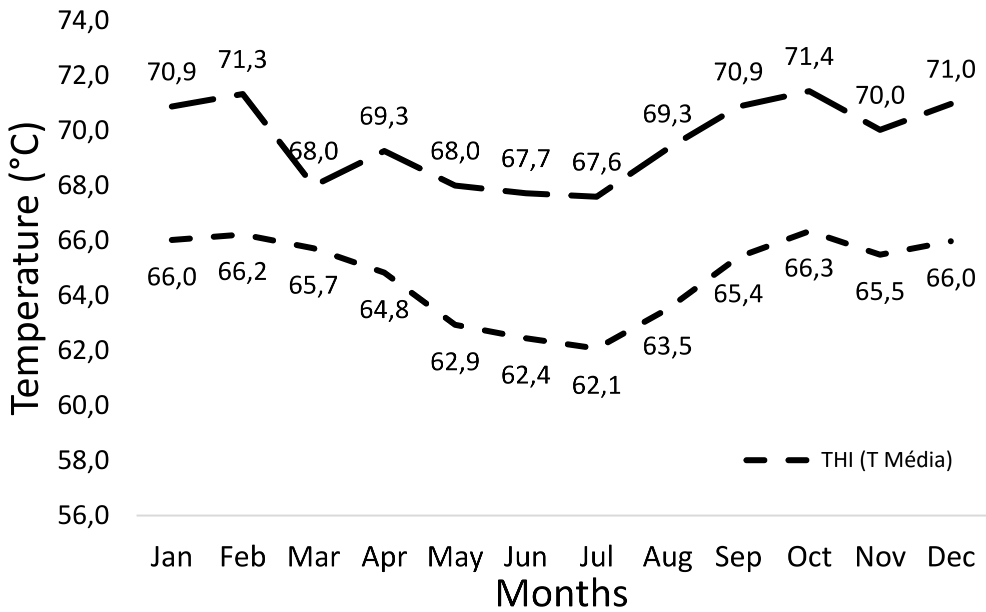
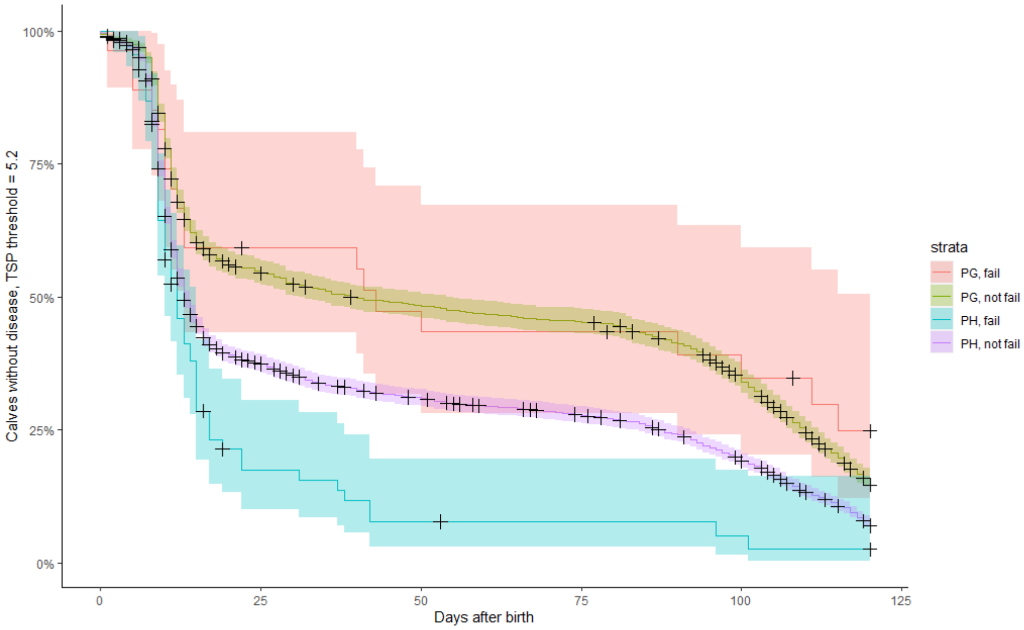
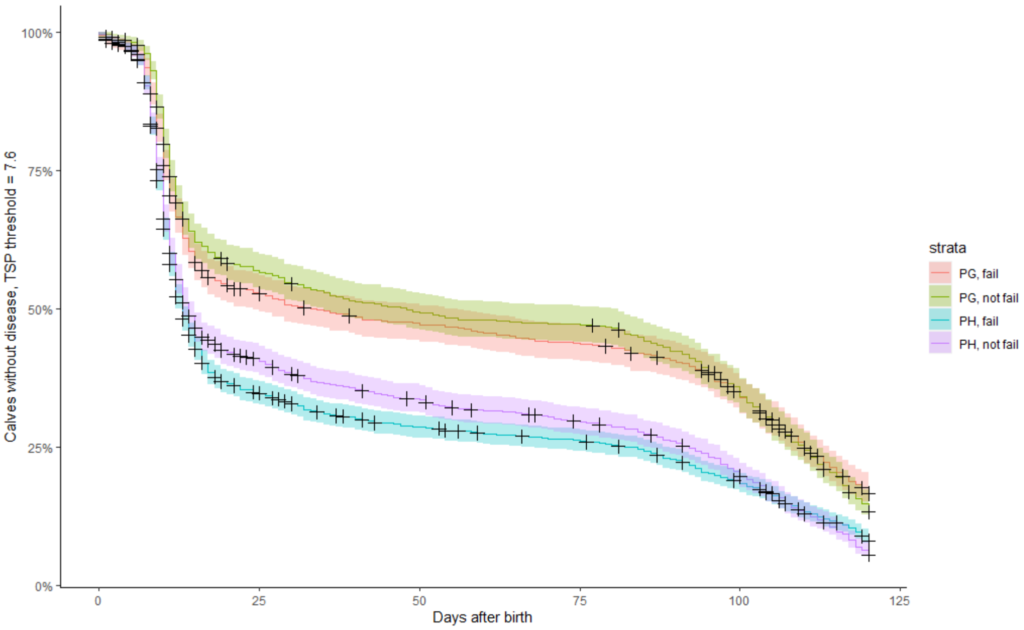


Figure 2. Average, minimum, and maximum annual temperature collected at Furnas weather station, located at 20 km from the dairy farm in southeast Brazil.

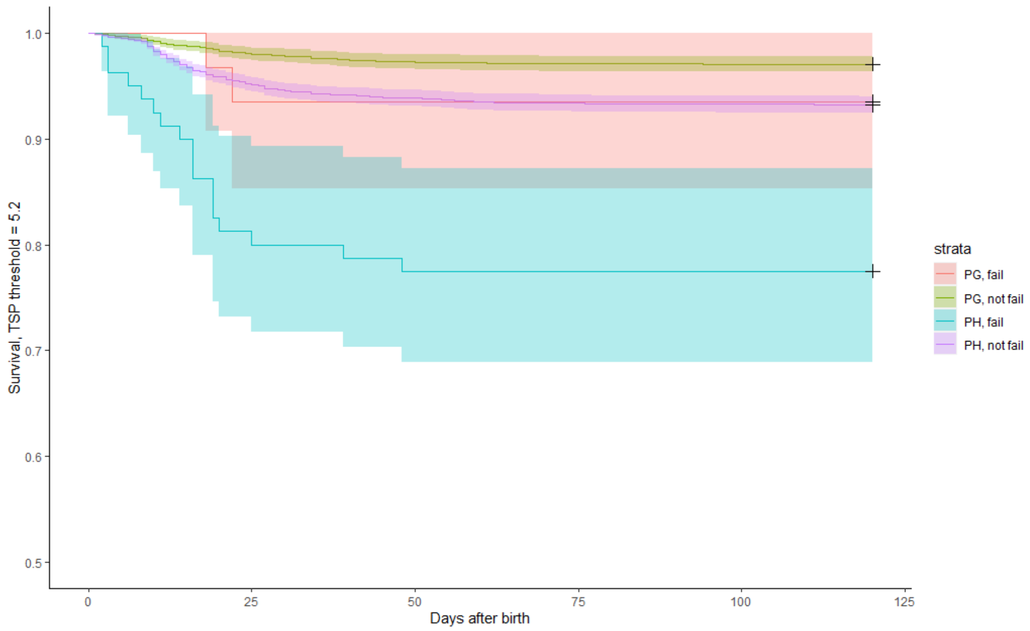


A

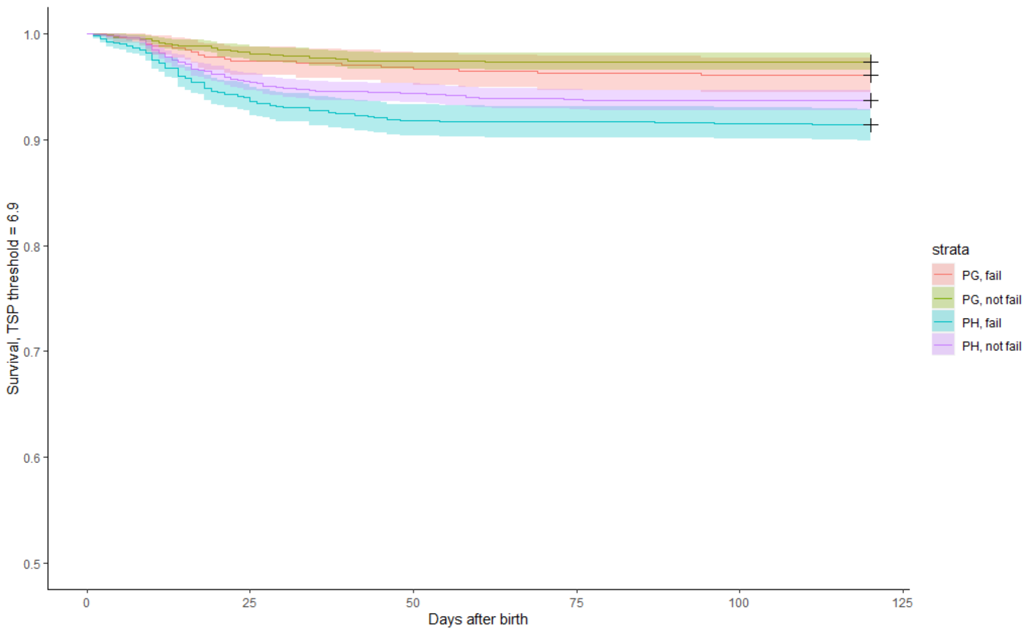


B

Figure 3. Morbidity probability by the failure of passive immune transfer (FTPI) at the thresholds for total serum protein (TSP) of 5.2 g/L (A) and 7.6 g/L (B) for pre-weaning dairy calves from a farm in southeast Brazil (n=6,011). PH: predominantly Holstein, PG: predominantly Gyr.



A



B

Figure 4. Survival probability by the failure of passive immune transfer (FTPI) at the thresholds for total serum protein (TSP) of 5.2 g/L (A) and 7.6 g/L (B) for pre-weaning dairy calves from a farm in southeast Brazil (n=6,011). PH: predominantly Holstein, PG: predominantly Gyr.