

Changes in Metabolism, Energy Reserves, and Gut Health in Newborn Piglets with Different Degrees of Intrauterine Growth Restriction

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This study evaluated morphological, physiological, and behavioral traits in piglets with varying birth weights (**BtW**) to identify early-life indicators associated with impaired growth and development, aiming to establish a classification system for piglets at birth according to the degree of intrauterine growth restriction (**IUGR**). A total of 1,990 crossbred piglets (Pietrain × [Landrace × Yorkshire]) were monitored from birth to weaning and classified according to BtW as follows: IUGR (BtW < 0.75 kg), restricted low BtW (**R-LBW**; BtW ≥ 0.75 and < 0.95 kg), non-restricted low BtW (**NR-LBW**; BtW ≥ 0.95 and < 1.15 kg), and normal BtW (**N**; BtW ≥ 1.15 kg). Piglets were assessed at birth for morphological, behavioral, and physiological traits, and colostrum intake and survival throughout lactation were recorded. Within 24 hours after birth, a subset of 48 piglets (12 per category) was euthanized for tissue collection and blood sampling. All euthanized IUGR piglets exhibited typical head morphological characteristics. Data were analyzed using ANOVA within a linear mixed-effects model, with piglet category as a fixed effect and sow as a random effect. The individual pig was considered the experimental unit. Metabolomics data were analyzed using the web-based platform MetaboAnalyst (<https://www.metaboanalyst.ca>). Significant differences in body weight (**BW**) from birth to weaning were observed among categories ($P < 0.001$). IUGR piglets exhibited the lowest BW, not differing from R-LBW piglets at day 7 and at weaning. Average daily gain was lower ($P \leq 0.027$) in IUGR and R-LBW piglets compared with NR-LBW and N piglets throughout lactation. IUGR piglets consumed the least colostrum ($P < 0.001$), averaging 208 g per piglet. Consequently, NR-LBW and N piglets exhibited greater serum immunoglobulin G concentrations than the other categories ($P \leq 0.028$). Vitality scores were lowest in IUGR piglets ($P < 0.001$), with 62.4% scoring the worst, corresponding to the highest mortality rate (78.5% during lactation). Serum albumin and insulin-like growth factor I concentrations were lowest in IUGR piglets and highest in N piglets ($P < 0.001$). Impaired amino acid and energy metabolism in IUGR piglets resulted in distinct metabolomic clustering compared with the other categories ($P \leq 0.008$). Liver glycogen concentrations differed among categories ($P = 0.014$), increasing linearly with BtW. Intestinal development and function were compromised in IUGR, R-LBW, and NR-LBW piglets, which

exhibited a lower villus height-to-crypt depth ratio compared with N piglets ($P \leq 0.029$), along with a gene expression profile characterized by the upregulation of pro-inflammatory and stress-related genes. In conclusion, IUGR piglets showed the most severe impairments in postnatal growth, vitality, and survival, associated with reduced colostrum intake, limited energy reserves, altered metabolic profiles, and gastrointestinal dysfunction. Differences between R-LBW and NR-LBW piglets, which also showed poorer growth performance than N piglets, were minimal.