

## Sex differences in metabolomic profile used for newborn screening

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Although it is now demonstrated that sex differences start in utero (Challis et al. 2013), a sex-gender approach in laboratory medicine is anyway scarce; furthermore, the influence of sex on acylcarnitines and amino acids levels at birth, which impacts on newborn screening, has not been thoroughly investigated. Newborn screening for inborn errors of metabolism is essential to reach a precocious diagnosis of aminoacidopathies, organic acidemias, and fatty acid oxidation disorders (Mak et al. 2013; Karam et al. 2013) and adequate reference ranges of blood amino acids and acylcarnitines are required for the diagnosis and management of inherited metabolic disorders.

Therefore, the present study aimed to establish the influence of sex on amino acids and acylcarnitines levels in male and female newborns.

Dried blood spots collected between 48 and 72 hours of life and amino acids and acylcarnitines were analysed using tandem mass spectrometry in 1856 male and 1824 female newborns. Data were analysed before and after body weight correction (which was significantly different between male and female neonates) also using a principal components analysis (PCA) (Raychaudhuri et al. 2000).

In this retrospective analytical study we showed that females had small but significantly higher levels of amino acids and the correction for body weight amplified these differences. Acylcarnitines were globally higher in males before body weight correction with the exception of C5, which was significantly higher in females and C4, which did not diverge between the sexes. Body weight correction decreased the sex differences in C5. PCA showed that both amino acids and acylcarnitines were necessary to describe the model for females, whereas only acylcarnitines were required for males.

These metabolomics data underline the importance of including sex as a variable in future investigations on circulating metabolites because they are deeply influenced by sex. The existence of sex differences highlights the need for distinct reference values for female and male neonates which also take account the body weight, for reach a precise diagnosis and management of inherited metabolic disorders which can significantly impact the clinical decision-making and quality of patient care.

Challis et al. *Placenta*;34:95-9, 2013

Mak et al. *Crit Rev Clin Lab Sci.*;50:142-62, 2013

Karam et al. *Clin Biochem.*;46:1787-92, 2013

Raychaudhuri et al. *Pac Symp Biocomput.* 455-66, 2000