

ASSOCIATIONS BETWEEN PRENATAL EXPOSURE TO A MIXTURE OF PHTHALATES, DINCH, AND HEAVY METALS AND NEONATAL BIRTH OUTCOMES: THE EXHES GREECE COHORT**Nafsika Papaioannou^{1,2}, Anthoula Chatzimpaloglou^{1,2}, Catherine Gabriel^{1,2}, Marios Maroulis^{2,4}, Maria Perikli^{2,4}, Spyros Karakitsios^{1,2}, Dimosthenis Sarigiannis^{1,2,3,5} ***

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ABSTRACT

Prenatal co-exposure to phthalates, Hexamoll® DINCH®, and metals are a societal concern due to their endocrine-disrupting properties. We aimed to investigate the associations of prenatal plasticizers and heavy metals co-exposure with birth outcomes in the EXHES study (n=60 pairs of mother-neonate from Greece). Pregnant women in the third trimester were recruited between 2020 to 2023 from Athens, Thessaloniki, Kavala, Kozani, Crete, Naoussa, Xanthi, Serres and Chalkidiki. 14 urinary phthalates (MEP, MBzP, MiBP, MnBP, MCHP, MnPeP, MEHP, 5OH-MEHP, 5oxo-MEHP, 5cx-MEHP, MnOP, OH-MiNP, cx-MiNP, and OH-MiDP) and 2 DINCH metabolites (OH-MINCH and cx-MINCH) were quantified using an online SPE LC-MS/MS method. The analytical method was optimized and validated in the ICI/EQUAS scheme organized by the HBM4EU initiative. 11 toxic and essential metals (As, Cd, Co, Cu, Mn, Ni, Pb, Se, V, Zn, and Hg) were also quantified in urine samples using an ICP-MS. The results were expressed as µg/g creatinine's. Neonatal birth outcomes, such as the gender of the newborn, gestational age, type of delivery, newborn weight (NW), length (NL), head circumference (NHC), Apgar score at 1 min (Apgar1), and 5 min (Apgar5), were measured by field nurse/physician or self-reported in questionnaires. We applied elastic net regression to identify important predictors and explored the chemical mixture's joint effects using BKMR. MEP was the most abundant phthalate metabolite (95th percentile 95.7), while As was the most abundant heavy metal (95th percentile 51.5). In addition, our study revealed that weight at birth was strongly associated with Hg and Mn. In conclusion, this was the first study to measure the prenatal co-exposure to 16 metabolites of plasticizers and 11 metals to assess the effects on birth outcomes, while covering north, central and south Greece.

KEYWORDS: exposome, phthalates, heavy metals, DINCH, environmental health