INTRODUCTION: Settleable atmospheric particulate matter (SePM), originating from industrial and urban activities, releases bioavailable metals and nanoparticles into aquatic environments. These contaminants, enriched with mining-related metals (e.g., Fe, Al, Ti, Mn, Zn, As) and rare earth elements, pose risks to aquatic organisms by disrupting osmoregulatory processes critical for homeostasis. **OBJECTIVE:** We utilized *Macrobrachium amazonicum* as a suitable model for investigating the physiological effects of metal mixtures under varying salinities. **MATERIALS AND METHODS:** Adult shrimps were purchased from local fishermen in Jau city, São Paulo, Brazil, and acclimated in freshwater (FW; <0.5‰) for 15 days and subsequently transferred either to brackish water (BW; 15‰) or maintained in FW. SePM exposure (1 $g \cdot L^{-1}$) was applied under both salinities (EFW and EBW groups) for 5 days at 25°C. Thereafter, they were cryoanesthetized by immersion in crushed ice for 5 minutes, and then the hemolymph was sampled by cardiac puncture, and the muscle, gills, and antennal gland were removed. Hemolymph osmolality, ion concentrations (Na^+, K^+, Cl^-, Mg^{2+}, Ca^{2+}), muscle hydration, and ATPase activities (Total ATPase, Na^+/K^+-ATPase [NKA], and $V(H^+)$-ATPase [VAT]) were analyzed. **RESULTS AND CONCLUSION**: The exposure to SePM in different salinities significantly affected shrimp osmo-ionic homeostasis. As expected, BW increased hemolymph osmolality and ionic concentrations, and decreased muscle hydration. SePM exposure, however, modified these parameters differently according to salinity, except for Mg^{2+}. SePM reduced Cl^- and Ca^{2+} concentrations in BW, potentially altering the resting membrane potential and impairing neuronal signaling. Calcium depletion may also compromise exoskeleton formation, affecting growth and molting. ATPase activities were differentially modulated. Total ATPase activity in the gills decreased by 17.6% following SePM exposure and 32.3% due to BW alone. VAT activity dropped significantly after SePM exposure, by 48.1% in FW and 33.5% in BW, while NKA activity remained unchanged across all treatments. Total ATPase and VAT inhibition contributed to the disruption in hemolymph osmo-ionic balance, with intensified effects under concurrent salinity and metal conditions. These physiological impairments could result in behavioral alterations and growth deficits. Since *M. amazonicum* requires brackish water for complete larval development, metal-induced disruptions in osmoregulation could have cascading consequences at the population level.