ABSTRACT: HIV viral load in pregnant and postpartum women is impacted by a diverse variety of factors and interventions to prevent perinatal transmission must take this into account. In this mixed-methods study, we examined the associations among various biomedical and socio-behavioral risk factors and high viral load (viral load > 1000 copies/mL) among 557 pregnant or postpartum women living with HIV enrolled in the Opt4Mama's study in western Kenya. Simple and multivariate logistic regression analysis was used to establish predictors of high viral load. An interdisciplinary team conducted case reviews of 40 participants with high viral loads and documented management recommendations. We then used thematic analysis to explore themes that arose in the case-reviews. High viral loads were associated with younger age (aOR 0.92, 95% CI [0.85, 0.99]), new HIV diagnosis (aOR 3.47, 95% CI [1.59, 33.21]), depression (aOR 2.56, 95% CI [1.59, 33.21]), and lower self-reported adherence (aOR 0.03, 95% CI [0.00, 0.16]). Thematic analysis of case review recommendations revealed four themes: multilevel contributing factors, drug change, adherence support, and psychosocial support. Psychosocial support was further divided into four sub-themes: socioeconomic, psychological, social, and disclosure support. Thematic analysis revealed that most women had multiple factors contributing to their high viral load indicating the multifactorial nature of HIV-related outcomes. All women who reported problems maintaining adherence were also reported to have psychosocial problems. Interventions were combined to address the unique contributing factors affecting women with high perinatal viral loads. A multifactorial approach to address the variety of socioecological challenges woman face is required to promote maternal health and facilitate perinatal HIV prevention.