Previous research on college campus environments, student mental health, and COVID-19 has primarily focused on individual-level factors, with limited attention to the broader institutional characteristics. Using the national survey data from the American College Health Association, this study examines the influence of both individual-level and institutional-level characteristics on college students’ stress, psychological distress, and psychological well-being, before and during COVID-19. The results indicate that: (1) COVID-19 significantly impacted students’ mental health; (2) institutional-level factors, such as school size, locale, region, and type, were significant predictors of mental health outcomes; and (3) individual-level variables, including gender, age, enrollment status, race, and GPA, moderated the relationship between COVID-19 and mental health. This study suggests the need to consider various institutional contexts in future efforts to understand predictors of mental health conditions and resilience.