Diarrhea is an important cause of morbidity and mortality in resource-poor settings. This study aims to characterize environmental drivers in transmission of enteric infections in 80 rural and 160 urban households in Vellore, India. Diarrheal episodes were investigated with microbiologic analysis of stool in an ongoing 1-year open cohort study. Information on demographics, hygiene, human/animal interactions, and water sources was collected by questionnaire. Household water contamination was tested using fecal coliform counts. Fly densities were measured in 2 seasons using fly ribbons placed in kitchens. PCR for enteric pathogens were performed on flies. From 8/6/2010-1/31/2011, there were 91 episodes of diarrhea over 198,795 total person days (PD) with substantial fluctuations in monthly incidence from 0.15 to 0.92 per 1000PD. Fecal coliforms were present in 67% and 74.6% of household water samples from rural and urban areas respectively. Stool pathogens isolated in 24 of 77 (31%) of samples included E.coli, Shigella spp., Vibrio spp., Giardia spp., Cryptosporidium spp., and rotavirus. 43 of 60 (72%) fly samples were positive for pathogens including E.coli, Salmonella spp., norovirus, and rotavirus. Fly densities were 2.56 times higher during the dry season compared to monsoon (p<0.001). The absence of animals in living quarters and indoor latrine use were protective of high fly densities. The adjusted relative risk of diarrhea associated with the 75th% of fly densities was 1.15 [95%CI:1.02,1.29]. Risk factors for increased duration of diarrhea included family size, private well or indoor house-tap use, untrimmed nails, and increased fly densities, while rural living, indoor latrines, no animals in living quarters, and better education were protective. Flies harbored enteric pathogens including norovirus, a poorly documented pathogen on flies. Several modifiable environmental risk factors for diarrhea were identified including water sources, living conditions, hygiene, and fly densities.