**Background/Aim:** Concern about adverse events and health costs of the inconsistent use of Stress Ulcer Prophylaxis (SUP) is increasing. This study aimed to evaluate SUP utilization and adherence to American Society of Health System Pharmacists (ASHP) guidelines.

Methods: The study was an observational retrospective study that was carried out in two Palestinian hospitals from September to November 2017. The medical records and medication sheets of a convenient sample from patients in ICU and internal units were reviewed. The results were analyzed using Statistical Package for Social Sciences (SPSS) program.

**Results:** A total of 337 patients were enrolled in this study, 170(50.45%) of them were females, 33.8% of the patients had hypertension. From the 337 cases, 274 case were prescribed SUP (81.3%) where the most common medications used were ranitidine in 135 (40.1%) and esomeprazole in 128 (38.0%). Among included patients, 225 (66.7%) had appropriate adherence to ASHP guideline during all days of hospital stay, while 103 (30.6%) patients received potentially inappropriate SUP as they had no risk factors or clear reasons for this use and 9 (2.6%) were not given SUP although they had risks.

Conclusion: This study shows potential overuse and misuse of SUP in ICUs and internal units which may cause unnecessary costs and adverse drug reactions. The rate of potential inappropriate use of SUP is lower than other studies. However, there is a room for improvement. The results highlight the need for interventions, including implementation of institutional protocols and prescribers' education.