To prospectively compare the results of palpation-guided fine needle aspiration biopsy (PG-FNAB) and ultrasound-guided fine needle aspiration biopsy (USG-FNAB) of thyroid nodules in an area of endemic goiter. Patients with solitary or multinodular goiter were included in this study. These patients underwent either PG-FNAB or USG-FNAB. The demographic and clinical characteristics and ultrasound findings of all patients were recorded. Each nodule was classified as mixed, cystic and solid. Patients with nodules smaller than 1 cm and larger than 4 cm were excluded. Regardless of whether the needle was guided by palpation or ultrasound, basic technique of thyroid FNAB was essentially the same for all procedures. All biopsy procedures were performed by a single physician and evaluated by the same cytopathologist. The results of both biopsy methods were statistically compared. Totally, 222 FNABs were obtained from 158 (133 females, 25 males) patients. There was no significant difference between the groups sampled with PG-FNAB (88) and USG-FNAB (134) for age, sex, hormonal status, TSH levels and ultrasound characteristics of nodules. The rate of diagnostic cytology was significantly higher in the USG-FNAB, whereas the number of nondiagnostic cytology was significantly higher in the PG-FNAB group (p=0.001). However, there was no significant difference between two groups for malignant cytology and suspicious malignant lesions. Routine USG-FNAB is superior than PG-FNAB for diagnostic yield and reducing unnecessary interventions, particularly for patients with multinodular goiter in an endemic goiter region. It is especially important that in endemic areas clinicians and family physicians should be informed of the epidemiological, clinical and laboratory features of brucellosis in order to prevent delayed diagnosis and complications. Furthermore, considering that the most important way of infection is still the use of unpasteurized milk products and animal farming, we believe that it is necessary to work on preventive measures.