Healthcare workers are at risk of medical sharps injuries, which according to the Kenya national policy on injection safety, 58% of healthcare workers have suffered these injuries. This study was conducted with the aim of establishing occupational risk factors contributing to injury by medical sharps among healthcare workers at Kenyatta National Hospital, Nairobi, Kenya. The objectives of this study were to; determine the frequency and severity of injuries from medical sharps; assess the risks due to exposure to medical sharps at the hospital, to ascertain the factors that contribute to occurrence of injury by medical sharps, and assess the measures in place to report, document, prevent, control, or manage injuries from medical sharps among health care workers. This descriptive cross sectional study was conducted between July and December 2010. A self administered questionnaire was distributed to 320 respondents from different job cadres of healthcare workers at the hospital who were selected proportionate to the sample frame. A checklist was used to observe medical sharps wastes management practices at the hospital. Focus group discussions were held with healthcare workers to obtain in-depth information on the root causes of medical sharps injuries at the hospital. Data were entered into MS Access database and analysis was done by use of Statistical Package for Social Sciences (SPSS), version 11.5. The study findings suggest that 44% of respondents were involved in medical sharps injury at the hospital. The majority of the injured respondents (91%) experienced medical sharps injuries between 1-2 times, while few of the respondents (5%) experienced medical sharps injuries 3-4 times within the past one year. Sixty two percent of injured respondents suffered moderate injuries which were characterized by skin puncture and some bleeding, while 33% of respondents suffered superficial injuries which were without any bleeding and 5% of respondents experienced severe injuries which were characterized by profuse bleeding. Many 75% of the injured respondents suffered a needle prick, 30% experienced a glove tear, while few 18% contracted upper respiratory tract infection, only 2% contracted pulmonary tuberculosis, and a paltry 0.3% of the respondents reported to be occupationally infected with Human Immunodeficiency virus, Hepatitis A and cellulites. The factors associated with medical sharps injury include; working in the critical care section (OR: 3.17, 95% CI: 1.4 7.2, p=0.01), working in the job cadre of a nurse (OR: 1.85, 95% CI: 1.16-2.95, p=0.01), and healthcare workers with education level of below diploma (OR: 1.85, 95% CI: 1.16-2.95, p=0.01). Seventy four percent of the respondents did not seek for post-exposure prophylaxis, while only 26% reported to have sought for post exposure prophylaxis. The research concluded that nurses were among healthcare workers at the highest risk of sharps injury, the critical care section presented more sharps injury risks than other sections at the hospital. Underreporting of medical sharps injury was common while many injured respondents did not seek for post exposure prophylaxis. There is need for adequate supply and use of safety engineered devices, safe disposal of medical sharps, better reporting and surveillance of sharps injury cases at the hospital.