with WHR, adiponectin, protein and vegetarian diet was also noted. These results may not be directly interpretable because of the possibility of mutual confounding.

Subsequently, crude and adjusted odds ratios for RCC were calculated for each increment of leptin, corresponding to one standard deviation among controls (Table 4). The unadjusted odds ratio for leptin was 0.65 (95% CI = 0.42-0.99, p = 0.04) and remained statistically significant after controlling for BMI, recent weight change, WHR, education level, physical activity, smoking, coffee and alcohol consumption, protein and vegetarian diet, DM and adiponectin.

**DISCUSSION**

An excess RCC risk was observed among patients with low circulating levels of leptin, after adjusting for potential confounding factors, such as central obesity, DM and adiponectin. Increased leptin levels have been associated with carcinogenesis in several organs, however, the mechanisms by which obesity promotes cancer development remain unknown. In our study, leptin levels were inversely associated with RCC risk and this association could be attributed in part to the weight loss due to disease; however, the dataset comprised newly diagnosed cases of RCC and the inverse association of leptin with RCC remained stable, even after controlling for confounding factors, including weight change. Therefore, we considered this association as primary. Given the immunogenic nature of RCC and the evident role of leptin in the regulation of immunocompetence, we opted to propose a theoretical pathogenetic mechanism that may link obesity, a state of chronic inflammation, with the immune system through leptin’s inter-talk with complex neuro-endocrine and other neural and immune circuits (Figure 1).

Leptin influences both innate and adaptive immunity. In obesity, monocytes/macrophages infiltrate adipose tissue and secrete proinflammatory cytokines,