Background: The relationship between obesity and hypertension is well established. However, the mechanisms through which obesity directly causes hypertension are still under investigation. The purpose of this study was to investigate the role of plasma inflammatory markers and adipokine levels in obese patients with and without hypertension and diabetes mellitus type 2 (DMT2). Subjects and Methods: A total of 377 (192 males and 185 females) Saudi adult subjects, aged 40-60 years, participated in this cross sectional study. Subjects were subdivided into four groups: healthy-non obese control, obese normotensive, obese hypertensive and obese hypertensive DMT2 patients. Fasting blood samples were collected and serum FBG, total cholesterol, triglycerides, HDL, leptin, adiponectin, resistin, insulin, TNF-α, CRP, PAI-1, CD163 and angiotensin II were measured. Results: Serum adiponectin concentration was lower in obese and obese hypertensive DMT2 than in control. Serum CRP levels were significantly elevated in obese, obese hypertensive and obese hypertensive DMT2 than in control group. Serum TNF-α was higher in obese hypertensive DMT2 and obese hypertensive than in control. Serum Ang II levels were elevated in obese, obese hypertensive and obese hypertensive DMT2 than in control. Serum PAI-1 was higher in obese hypertensive DMT2 than in control. Serum soluble CD163 was higher in obese than control. Systolic blood pressure was positively associated with BMI, Glucose, Insulin, HOMA-IR, TNF-α, and PAI-1. A significant association was found between elevated levels of TNF-alpha and risk of hypertension [OR (95% CI), 1.96 (1.26, 3.05)]. TNF-α was the sole significant predictor of blood pressure. Conclusion: Serum adiponectin, CRP, soluble CD163 and TNF-alpha are altered among obese, and obese hypertensive subjects, suggesting a mechanistic role of inflammatory markers and adipokines in the pathogenesis of obesity-related hypertension.