Need
Of
Present Investigation
2. Need for the study:

The global figure of people with diabetes is set to rise from the current estimate of 150 million to 220 million in 2010, and 300 million in 2025 (Hussain et al., 2001). The 21st century has the most diabetogenic environment in human history (Atkins et al., 2003; Brussels; 2003). Over the past 25 years or so, the prevalence of type 2 diabetes in the USA has almost doubled, with three- to five-fold increases in India, Indonesia, China, Korea and Thailand (Zimmet et al., 2004). In 2007, there were 246 million people with diabetes in the world, but by 2025, that number is estimated to reach 380 million (King et al., 1998). People with impaired glucose tolerance, a “prediabetic state” numbered 308 million in 2007 and will increase to 418 million by 2025 (King et al., 1998). The increase in prevalence of diabetes will be greater in the developing countries. According to the WHO, China and India will have about 130 million diabetics by 2025 who will consume about 40% of their country’s healthcare budget in addition to reducing productivity and hindering economic growth. It was against this background that on December 21st 2006, the United Nations General Assembly unanimously passed Resolution 61/225 declaring diabetes an international public health issue and identifying World Diabetes Day as a United Nations Day, only the second disease after HIV/AIDS to attain that status.

Diabetes is now the major cause of end stage kidney failure throughout the world in both developed and emerging nations (Yoon et al., 2006). Between 1983 and 2005, there was a 7-fold increase in new patients starting renal replacement therapy in Japan because of diabetes, accounting for 40% of all new incidence patients (Bethesda, 2007). Thus, some 30% of the predicted 1.1 trillion dollar medical costs of dialysis world-wide during this decade will result from diabetic nephropathy (McDonalde et al., 2008). In the United Kingdom Prospective Diabetes Study (UKPDS), the rates of progression of newly diagnosed type 2 diabetics between the stages of normoalbuminuria, microalbuminuria, macroalbuminuria and renal failure were 2 – 3% per year (Yamagata et al., 2008).

Over a median of 15 years of follow-up of 4,000 participants, almost 40% developed microalbuminuria.12 In the DEMAND study of 32,208 people from 33 countries with known type 2 diabetes attending their family doctor, 39% had microalbuminuria and prevalence increased with age, duration of diabetes and presence of hypertension) (Adler et al., 2003). About 30% of the
UKPDS cohort developed renal impairment, of which almost 50% did not have preceding albuminuria (Lysaght. 2002). Reduced glomerular filtration rate and albuminuria caused by diabetic nephropathy are independent risk factors for cardiovascular events and death (Retnakaran et al., 2006).

Hence, Diabetic nephropathy (DN) remains the most common cause for end stage renal disease (ESRD) as the burden of diabetes increases worldwide. Nearly one-third of patients with diabetes develop nephropathy making early diagnosis critical in preventing long term kidney loss (Choudhury et al., 2010).

Lifetime risk for developing DN with progression to ESRD is roughly equivalent in type 1 and type 2 diabetes (Ritz and Orth, 1999). Presence of DN heralds a marked increase in patient morbidity and premature mortality, and significantly impacts cost of care (White et al., 2008). While mortality with diabetic renal disease can precede progression to ESRD, diabetes in those with ESRD remains a significant predictor for increased cardiovascular risk and mortality (National Institute of Diabetes and Digestive and Kidney Diseases, 2010). For these reasons, a focus on exploring new treatment options is relevant and the goal for this study.

Moreso, in the past, there was much discussion about the specific renal benefit provided by ACE inhibition. The meta-analysis of Jafar et al. showed clearly that ACE inhibitors are only superior to alternative antihypertensive treatments in patients that have proteinuria >1 g/day. In nonproteinuric patients, a specific benefit from blocking the RAS pathway is not well documented. Furthermore, the analysis of Pohl et al. in the IDNT study showed that lowering blood pressure has a much greater impact on renal end points than the blocking of RAS with irbesartan. A major problem with blocking the RAS pathway is the phenomenon of escape, i.e., the return of protein excretion to baseline values after months or years.