Summary and conclusion

The aim of this work was to study the role of tumor necrosis factor alpha (TNF -α) in the pathogenesis of diabetic nephropathy and its predictor value for early detection of diabetic nephropathy.

This study was conducted on eighty-five individuals, divided into, four groups:

group I :twenty five type II diabetic patients without albumin in urine.

group II: twenty five type II diabetic patients with microalbuminurea **.**

group III: twenty five type II diabetic patients with macroalbuminurea.

control group: ten healthy individuals .

They were selected from outpatient and inpatient clinics, Banha University Hospital.

All individuals were subjected to the following:

full history taking , complete clinical examination , laboratory investigations including:

1- Complete blood count **.**
2- Fasting and post prandial blood glucose **.**
3- Glycated hemoglobin .
4- Serum lipid {Cholesterol, Triglyceride**,** HDL and LDL).
5- Blood urea and serum creatinine **.**
6- Complete urine analysis .
7- Estimation of serum c- reactive protein **. .**
8- Estimation of micro albumin in urine **.**

9- Estimation of serum tumor necrosis factor alpha**.**

10-Estimation of tumor necrosis factor alpha in urine .

This study revealed the following:

- Serum CRP (mg/l) significantly elevated in all diabetic groups compared to the control group (4± 1.53)

- Serum CRP(mg/l) significantly elevated in macroalbuminuric (20.48±8.72) group compared to microalbuminuric (16.24±6.20) ,and normoalbuminuric (8.86±3.45)groups.

- Serum TNF –α (pg/ml) significantly elevated in microalbuminuric (6.79±3.52) and macroalbuminuric (7.39±4.24) groups compared to the control group (2.18± 1.85), p< 0.001, but the elevation in normoalbuminuric group (2.53 ± 1.65) was not statistically significant p.>0.05.

- Serum TNF-α (pg/ml) significantly elevated in macroalbuminuric (7.39±4.24) and microalbuminuric (6.79±3.52) groups compared to normoalbuminuric group(2.53 ± 1.65) But there was no statistically significant difference in serum TNF-α between macroalbuminuric and microalbuminuric group

- Urinary TNF -α (pg/mg) significantly elevated in all diabetic groups compared to the control group (3.77±3.32) ,p< 0.001

- Urinary TNF -α (pg/mg) significantly elevated in macroalbuminuric group (19.63±6.67) compared to microalbuminuric (13.36±4.88), and normoalbuminuric groups(7.91±3.65) p< 0.001..Also it was significantly elevated in microalbuminuric group compared to normoalbuminuric group p< 0.001.
- Duration of diabetes mellitus (years) significantly longer in macroalbuminuric (11.92±4.28) group compared to microalbuminuric(8±3.42) and normoalbuminuric (5.88 ± 2.11), groups , p< 0.001

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- Systolic blood pressure (mmHg) significantly higher in macroalbuminuric group (152±6.92) compared to microalbuminuric(141.4±7) and normoalbuminuric groups (135.2±8.48), p< 0.001

- Diastolic blood pressure (mmHg) significantly higher in macroalbuminuric (96.2±6.96) and microalbuminuric groups (86.8±6.44) compared with normoalbuminuric group (84±5.2), p< 0.001

- Fasting blood sugar, postprandial blood sugar (mg/dl) and glycated Hb (%)significantly higher in macroalbuminuric (193.24±55.14) (267.96±75.02) (8.48±0.63) compared with normoalbuminuric group (153.28±37.11) (216.36±56.65) (7.38±0.77) respectively p< 0.001

- 24 hour urinary albumin excretion (UAE**)** (mg/d)significantly elevated in macroalbuminuric (851.2±126.96) group compared to

microalbuminuric (123.8±66.63) and normoalbuminuric (14.16±7.41) groups also it was significantly elevated in microalbuminuric compared with normoalbuminuric group p< 0.001.

- blood urea (mg/dl) significantly elevated in macroalbuminuric (53.67±17.99) group compared to microalbuminuric (34.96±8.93) and normoalbuminuric(33.86±5.41) groups p< 0.001.
- Serum creatinine (mg/dl) significantly elevated in macroalbuminuric (1.81±0.76) group compared to microalbuminuric (1.05±0.27) and normoalbuminuric((1.06 ± 0.24), groups p< 0.001.

- Triglyceride (mg/dl) significantly higher in macroalbuminuric (125.82±20.15) and microalbuminuric (122.96±16.03) groups compared with normoalbuminuric group (99.38±12.82), p<0.001

- HDL (mg/dl) significantly lower in macroalbuminuric (31.06±5.44) compared with microalbuminuric(37.2±4.72) and normoalbuminuric (39.1±7.26), groups ,p<0.001

- There was no significant correlation between CRP and age, diastolic blood pressure Cholesterol, LDL, HDL ,p>0.05. While there was significant positive correlation between CRP and duration of diabetes, systolic blood pressure, fasting blood glucose, Postprandial blood glucose, glycated Hb, triglycerides, proteinurea, serum TNF- α, and urinary TNF- α, p< 0.05.
- There was no significant correlation between serum TNF- α, and age, diastolic blood pressure, fasting blood glucose, postprandial blood

glucose, Cholesterol, LDL, HDL, urinary TNF- α, p>0.05.. While there was significant positive correlation between serum TNF- α, and duration of diabetes, systolic blood pressure, glycated Hb, triglycerides and proteinurea , p< 0.05.

- There was no significant correlation between urinary TNF- α, and age, diastolic blood pressure, Cholesterol, LDL, and HDL p>0.05.. While there was significant positive correlation between urinary TNF- α, and duration of diabetes, systolic blood pressure, fasting blood glucose, Postprandial blood glucose, glycated Hb, triglycerides and proteinurea , p< 0.05.

Conclusion:

CRP, serum and urinary TNF- α were significantly greater in diabetic patients than controls means that diabetes mellitus is associated with systemic inflammation ,also its levels increased significantly as nephropathy progressed**.** In addition, these parameters were independently related to UAE at early stages of nephropathy in patients with type 2 diabetes suggesting that it could be a predictor for nephropathy. The lack of association between serum and urinary TNF-a levels indicates, that TNF- α can be produced in the kidney, this indicates that inflammation may be a pathogenic mechanism of diabetic nephropathy. Thus, it is possible to hypothesize on the participation of locally released cytokines, such as TNF-α in the development of renal damage through several mechanisms , such as direct cellular injury , alteration of the glomerular protein permeability barrier , and development of intrarenal inflammatory reactions

Recommendation:

Further studies of TNF-α in gene polymorphism in diabetic nephropathy is recommended, also additional studies about anti TNF-α as a new therapeutic target for prevention and treatment of diabetic nephropathy.