

# EFFECT OF GENDER AND DIABETES IN CIRCULATING AND RENAL ACE AND ACE2 IN STREPTOZOTOCIN-INDUCED MICE

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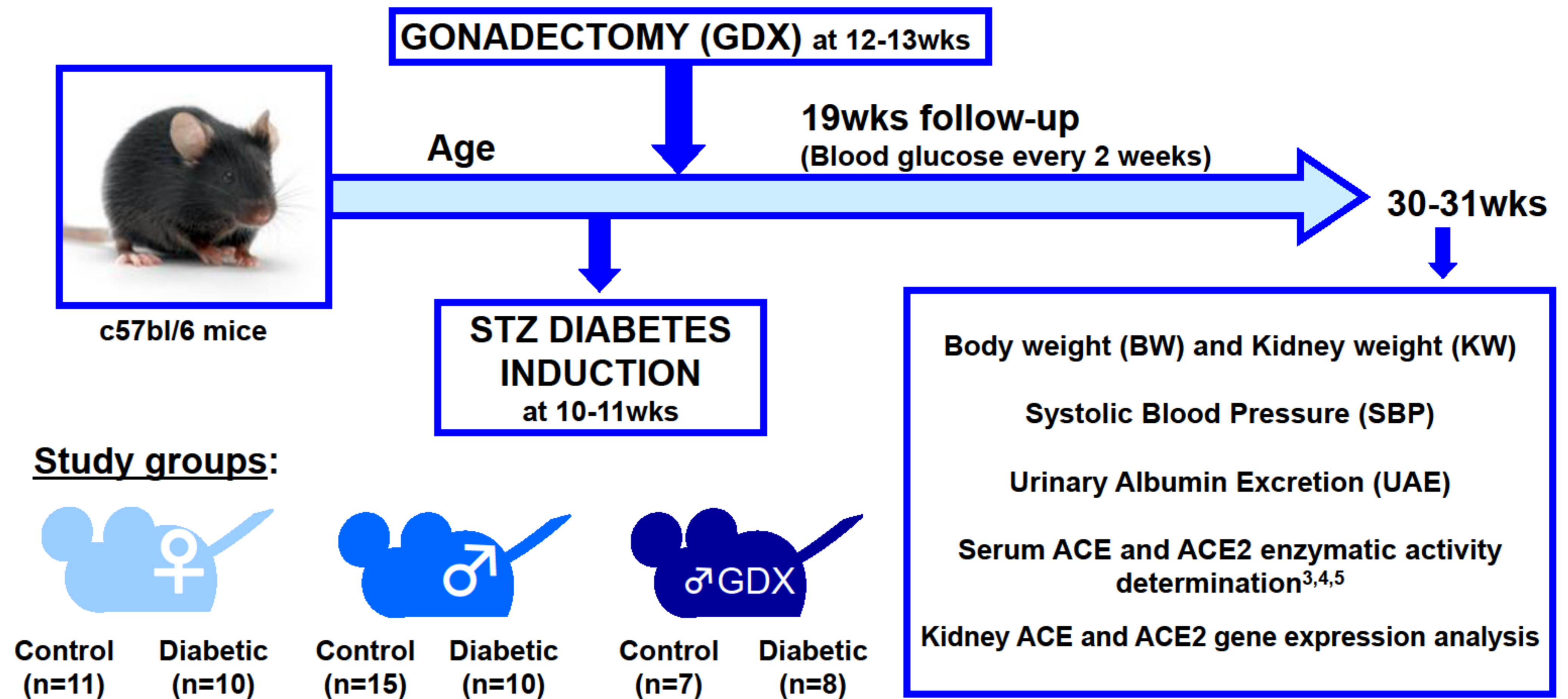
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## INTRODUCTION & AIM

- Male gender predisposes to chronic kidney disease<sup>1</sup>.
- We previously showed that circulating ACE and ACE2 activities are increased in diabetic male mice<sup>2</sup>.
- We proposed to study gender and the effect of diabetes in the streptozotocin (STZ) mice in circulating and renal ACE and ACE2. We also studied the effect of gonadectomy in diabetic and control mice.

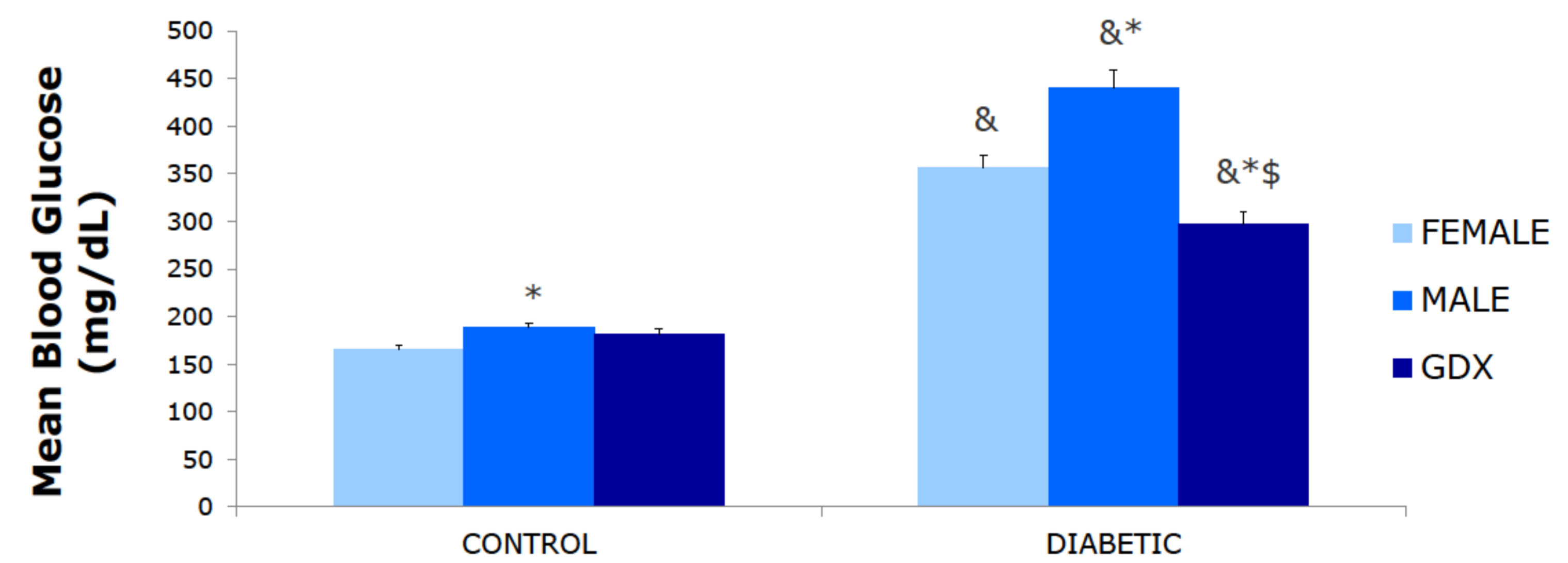
## METHODS



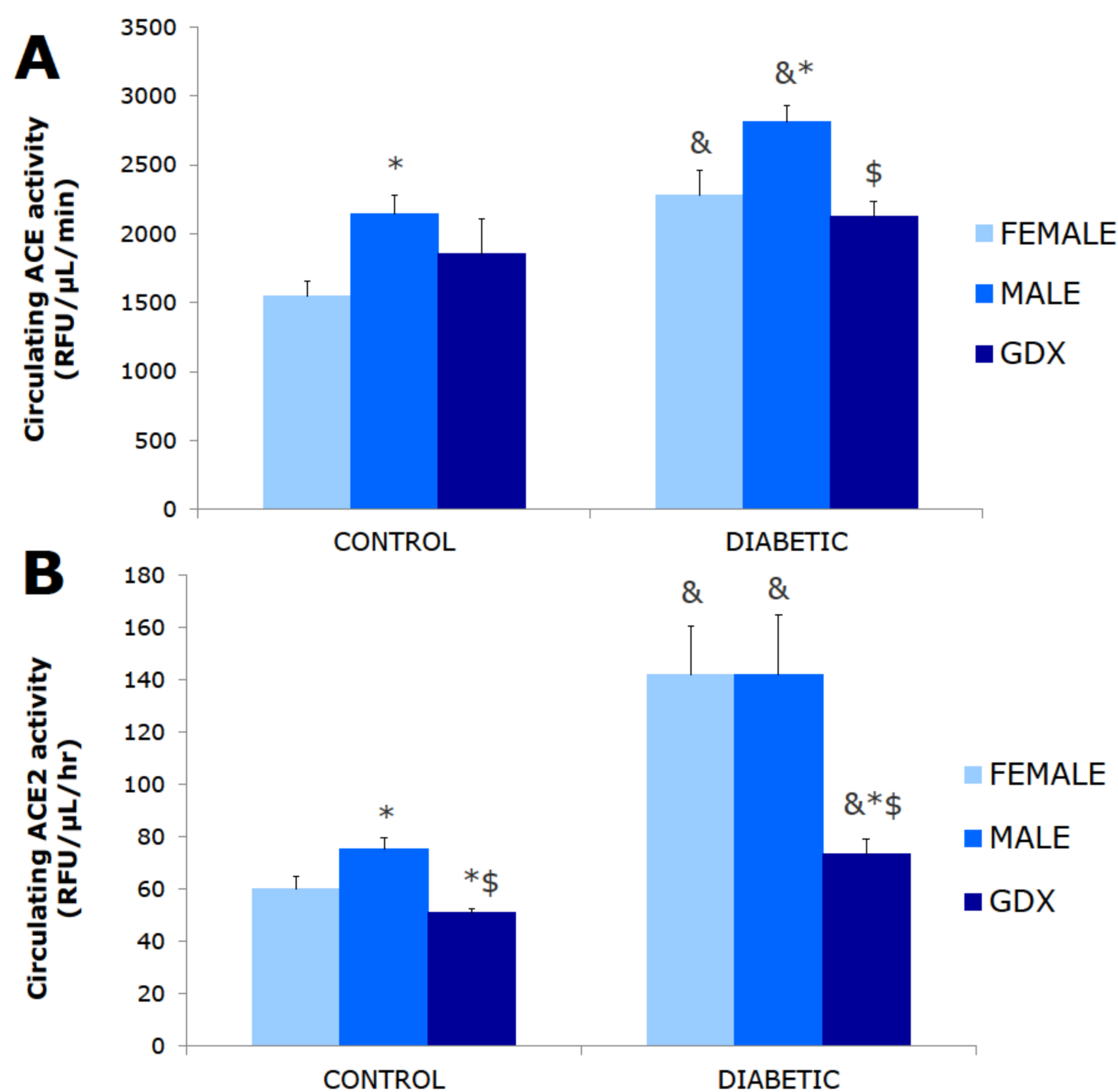
## RESULTS

|                         | Age (wks)  | Body weight (gr) | %KW/BW       | SBP (mmHg)  | UAE (µgAlb/mgCrea) |
|-------------------------|------------|------------------|--------------|-------------|--------------------|
| <b>CONTROL FEMALES</b>  | 30.78±0.20 | 26.75±0.95       | 0.91±0.02    | 98.22±2.11  | 14.76±3.16         |
| <b>CONTROL MALES</b>    | 30.31±0.12 | 36.61±1.00*      | 0.97±0.03*   | 96.37±1.63  | 18.47±2.46         |
| <b>CONTROL GDX</b>      | 30.06±0.30 | 30.32±0.94*‡     | 0.79±0.03*‡  | 100.14±2.11 | 19.57±7.90         |
| <b>DIABETIC FEMALES</b> | 30.64±0.24 | 21.56±0.56&      | 1.44±0.08&   | 106±3.81    | 86.43±26.25&       |
| <b>DIABETIC MALES</b>   | 30.30±0.23 | 26.79±0.82*‡     | 1.32±0.06&   | 96.63±1.88* | 308.03±133.89*‡    |
| <b>DIABETIC GDX</b>     | 30.05±0.22 | 24.96±0.58*‡§    | 0.89±0.02*‡§ | 97.79±1.68  | 22.21±5.65‡        |

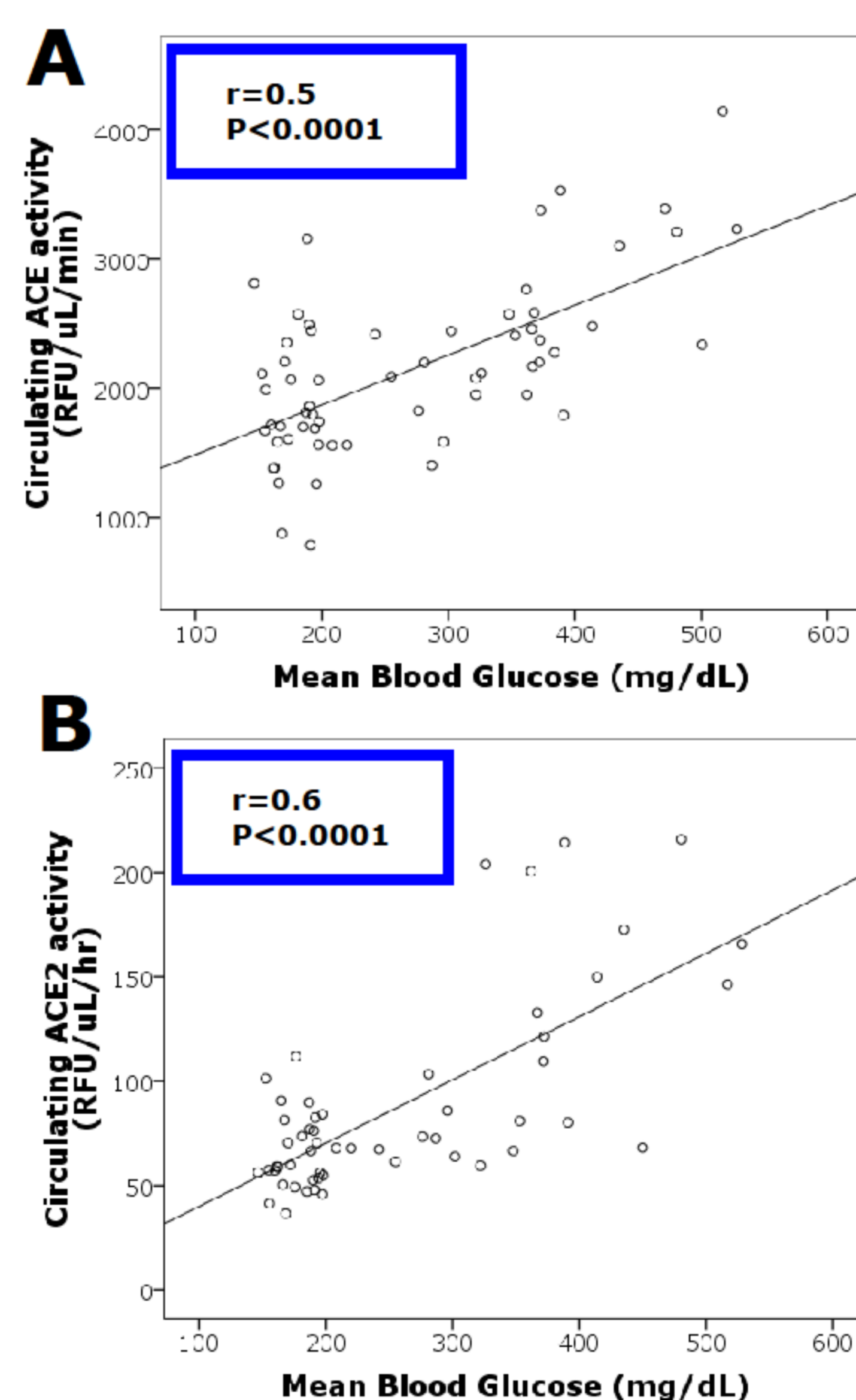
**Table 1. Animal characteristics at the end of the study.** All diabetic groups showed significantly lower body weight and higher % of kidney weight respect to body weight (%KW/BW) as compared to their controls. Gonadectomy significantly decreased body weight and %KW/BW in both control and diabetic male mice. \*p<0.05 vs. FEMALE; ‡p<0.05 vs. MALE; &p<0.05 vs. CONTROL.



**Figure 1. Mean Blood Glucose during the follow-up.** Hyperglycemia was observed in all STZ groups. Mean Blood Glucose (BG) was significantly higher in males as compared to females for both control and diabetic groups. Furthermore, gonadectomy significantly decreased hyperglycemia in the diabetic mice.

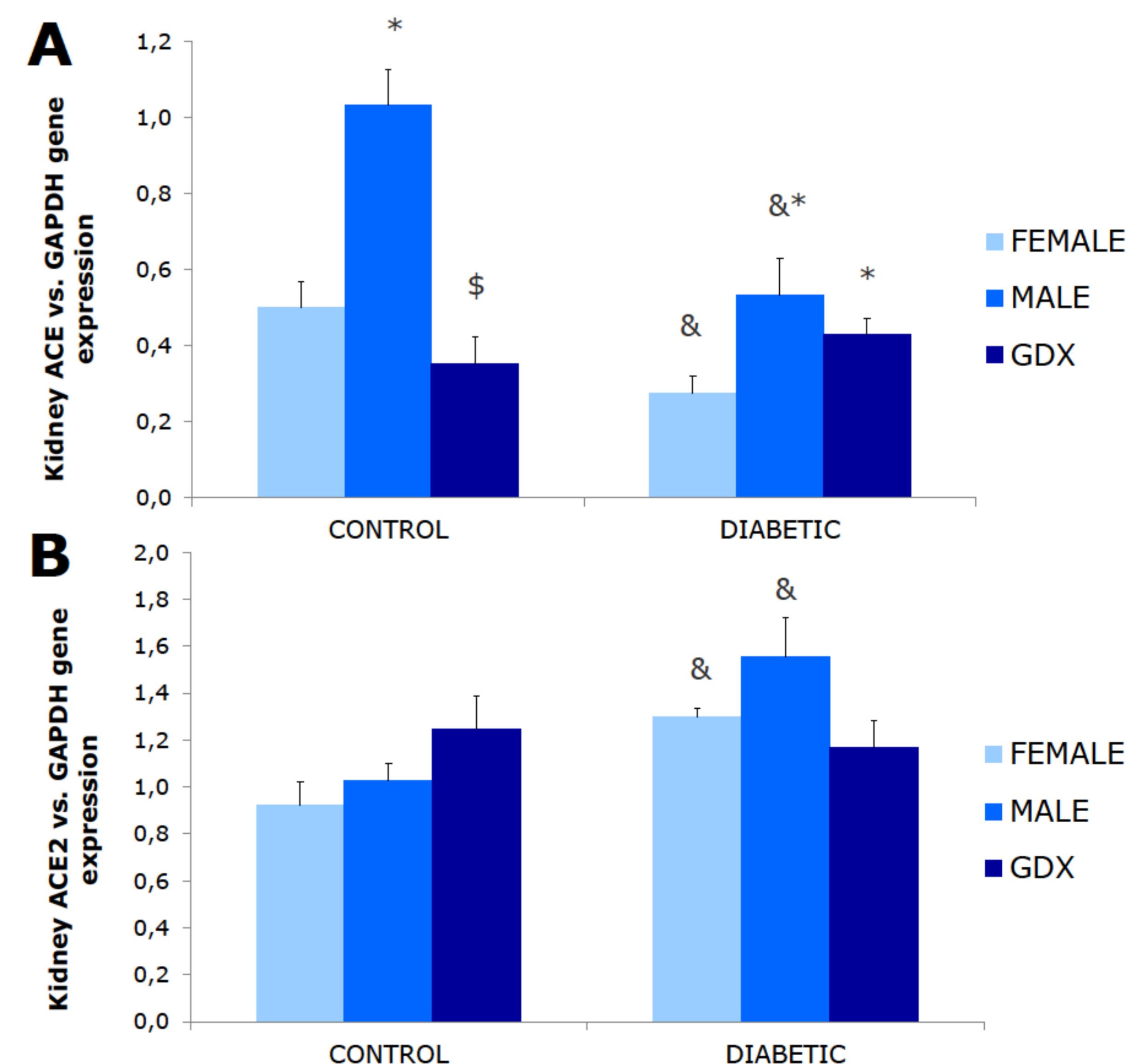


**Figure 2. Circulating ACE and ACE2 enzymatic activities at the end of the study.** Circulating ACE and ACE2 activities were increased in both male and female diabetic mice compared to their controls. Male control mice showed significantly higher serum ACE and ACE2 than females. Gdx resulted in significant reduction of serum ACE2 (in control and diabetic males) and ACE (only in diabetic males).



**Figure 3. Correlations.** Direct correlations between blood glucose and circulating ACE (A) and ACE2 (B) activities were found.

\* p<0.05 vs. FEMALE; ‡ p<0.05 vs. MALE; & p<0.05 vs. CONTROL



**Figure 4. Renal cortex ACE (A) and ACE2 (B) gene expression at the end of the study.** Diabetes increased renal ACE2 but decreased ACE gene expression in both male and female mice. In addition, kidney ACE was augmented in both control and diabetic male mice as compared to females. This increase was reduced by Gdx in control males.

## CONCLUSIONS

- Increased BG in diabetic mice was accompanied by higher circulating ACE and ACE2 activities in all diabetic groups.
- In addition, increased kidney ACE2 and decreased kidney ACE gene expression were observed in diabetic males and females.
- Gdx decreased BG, circulating ACE2 and circulating and renal ACE.
- These ACE and ACE2 alterations observed in diabetic male mice at serum and kidney level may be ascribed to a dysregulation of male sex hormones in type 1 diabetes.

## REFERENCES

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