THROMBO-INFLAMMATORY BIOMARKERS OF CARDIORENAL SYNDROME IN PATIENTS UNDERGOING MAINTENANCE HEMODIALYSIS IN END-STAGE RENAL DISEASE

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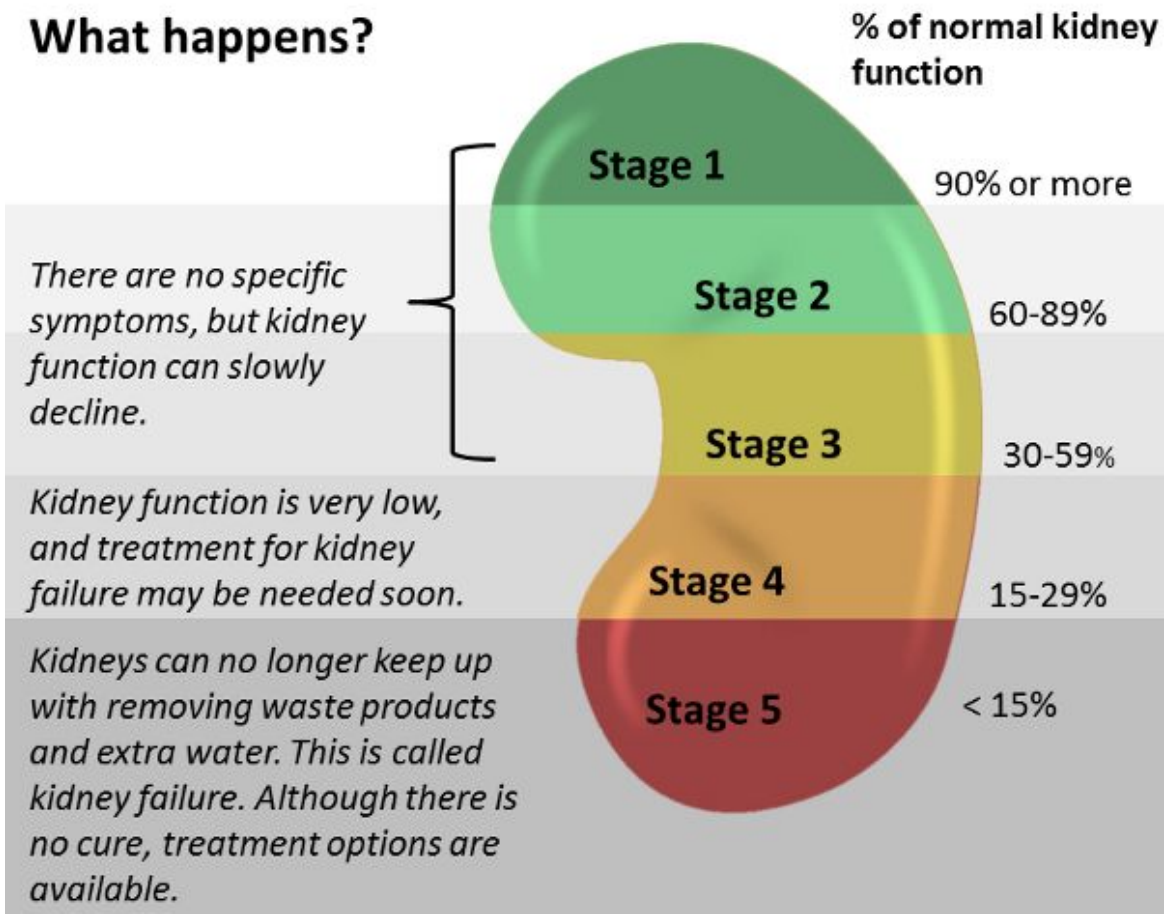
INTRODUCTION

- End-stage renal disease (ESRD) is the final stage of chronic kidney disease
- ESRD requires dialysis or kidney transplant as treatment
- 131,636 documented cases of ESRD in the United States as of 2018
- Further research and increasing treatment availability is decreasing ESRD mortality rate
- Thrombo-inflammatory biomarkers are biochemical molecules which indicate the presence of thrombosis and/or inflammation in one's body
  - D-dimer, TNF-a, IL-6

STAGES OF CHRONIC KIDNEY DISEASE



HYPOTHESIS AND AIMS

Hypothesis: Circulating levels of thrombo-inflammatory biomarkers of kidney disfunction may be elevated in ESRD patients

Aims:

1) To analyze concentrations of thrombo-inflammatory biomarkers in ESRD patients compared to the general population, and their role in the development of ESRD.

2) To profile D-dimer, IL-6, and TNF-a in ESRD patients.

3) To identify ESRD patient population based on biomarker signature and laboratory parameters.

MATERIALS AND METHOD

- 95 ESRD patient plasma samples were used.
- Samples were centrifuged to produce platelet poor plasma, aliquoted, and frozen at -80 degrees Celsius.
- Sandwich ELISA kits were used to measure levels of D-dimer, IL-6, and TNF-α in the ESRD patients' blood plasma samples.
- 50 samples of normal human plasma (NHP), commercially obtained from a centralized blood bank, served as a control group for comparison.
- Data was analyzed using PRISM GraphPad and IBM SPSS
- Two-tailed t-tests, Mann-Whitney tests, tests for normal distribution, skewness analyses, and correlation analyses were conducted to determine correlation and statistical significance
- Statistical significance was defined as $p < 0.05$

BIOMARKERS

D-DIMER

- Fibrin degradation product
- Small protein fragment in the blood after the degradation of a blood clot by fibrinolysis
- Concentration of D-dimer can be found through a blood test and can help diagnose thrombosis
  - Positive D-dimer can indicate abnormally high levels of fibrin degradation products
- Indicates thrombus formation and breakdown is occurring somewhere in the body, but does not indicate where exactly it is occurring
- Used as a screening test because it is good at detecting clots but does not indicate if the clot is clinically significant

IL-6

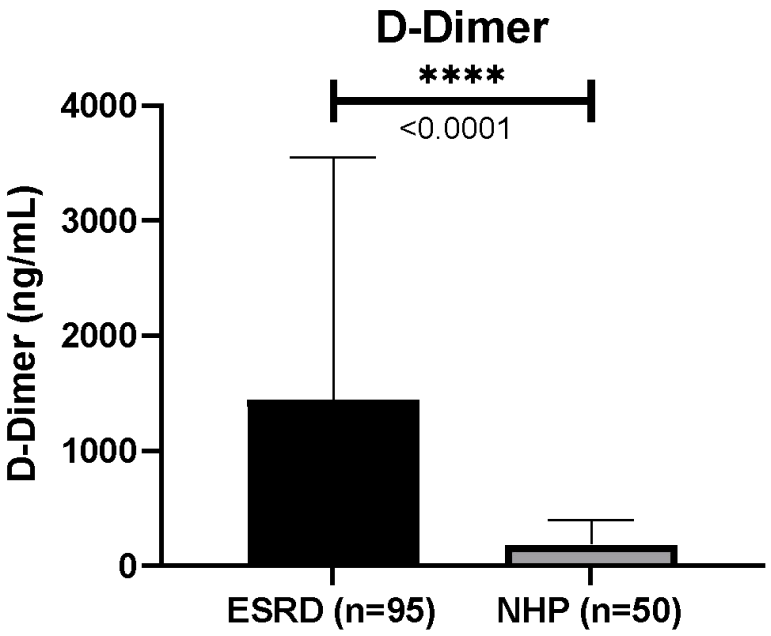
- Secreted by macrophages
- Secreted in response to bacterial infection from specific microbial molecules
- Mediator of acute inflammation and fever
- Supports growth of B cells
- Important in regulation of B cell function
- Responsible for stimulating production of neutrophils in bone marrow
- Stimulates autoimmune and inflammatory process in several diseases
    - Multiple sclerosis, atherosclerosis, lupus, rheumatoid arthritis

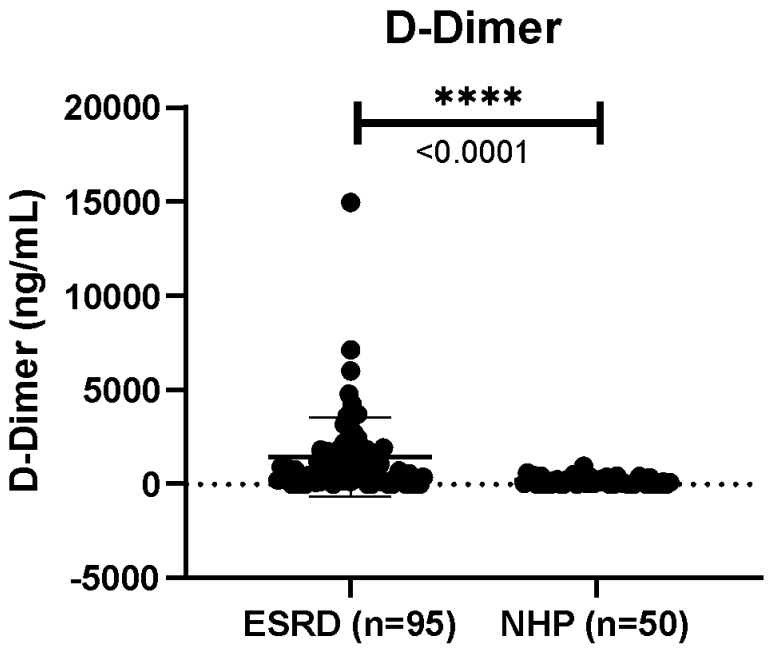
TUMOR NECROSIS FACTOR ALPHA (TNF-A)

- Inflammatory molecule
- Produced during acute inflammation by macrophages/monocytes
- Responsible for many signaling events in cells
  - Leads to apoptosis (cell death)
- Important for resistance to infection and cancers
- Important in regulation of B cell function

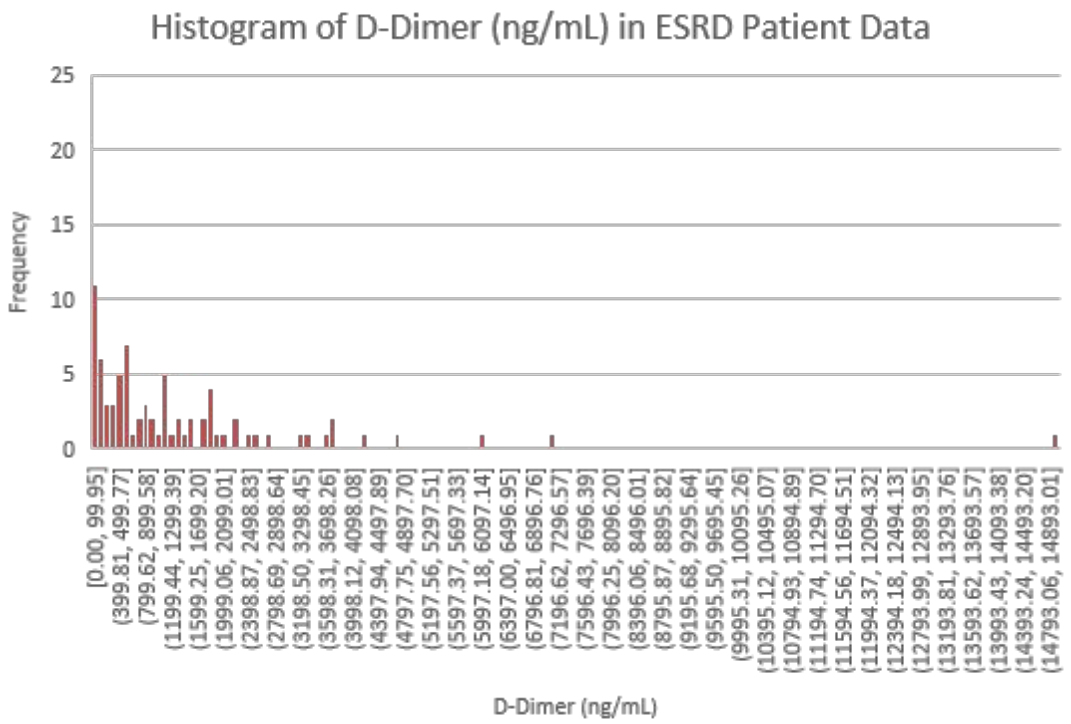
RESULTS

D-DIMER DATA ANALYSIS





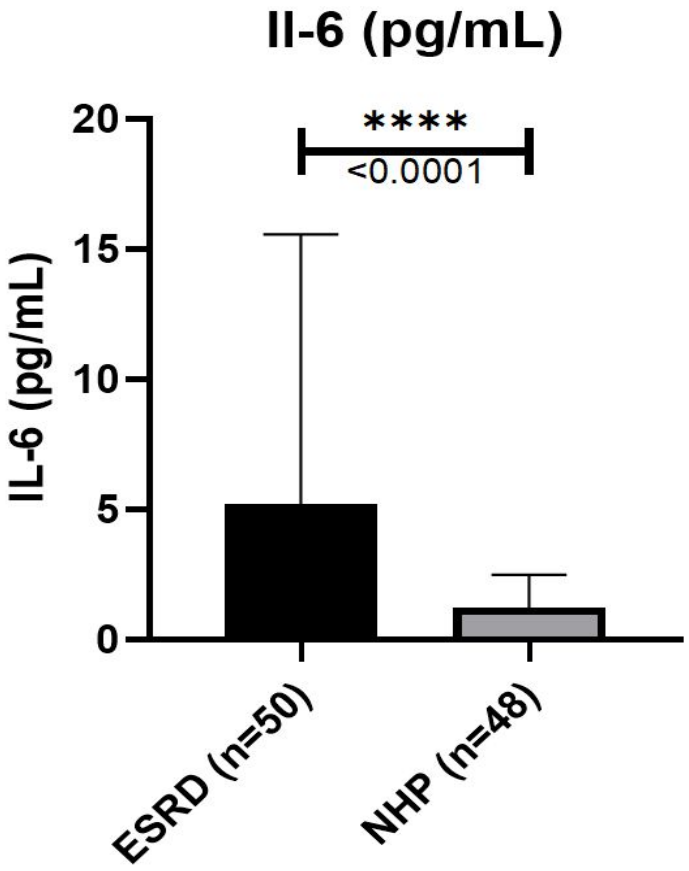
D-DIMER DATA ANALYSIS

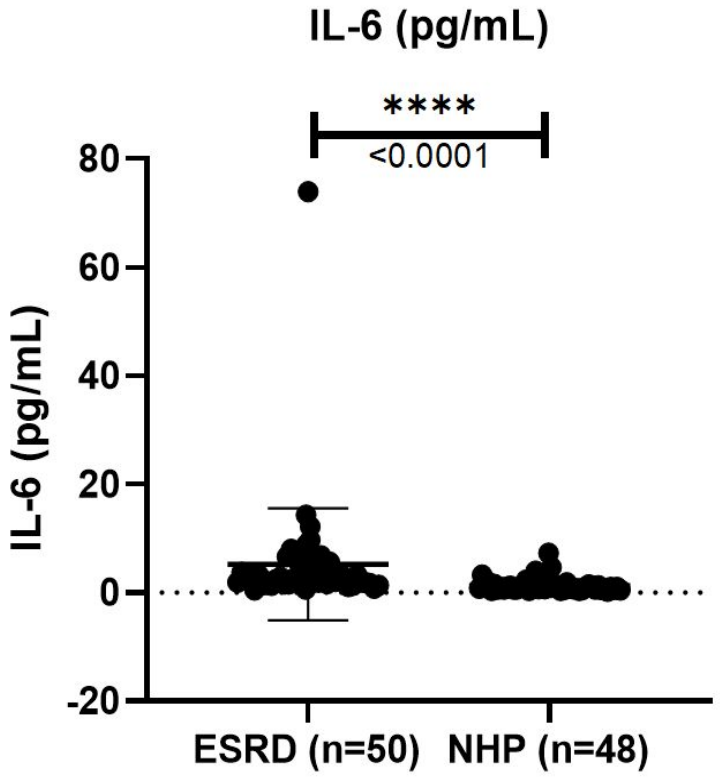


	ESRD Data (ng/mL)	Control Data (ng/mL)
Average	1447.01	187.726
SD	2103.2934	212.4925
SEM	215.7933	30.0501
Min	0.00	0.00
Max	14992.96	960.8527
% Change of Mean	**670.8096%**	

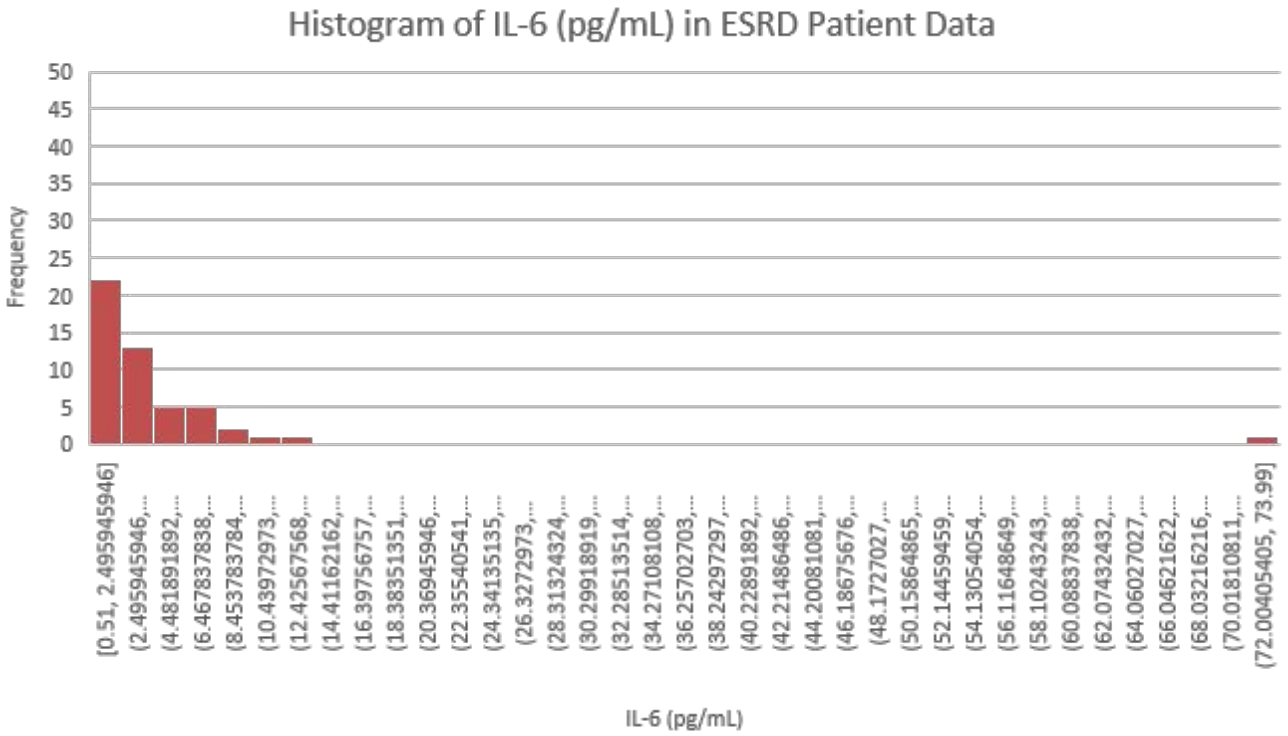
- Skewness = 2.587

IL-6 DATA ANALYSIS





IL-6 DATA ANALYSIS

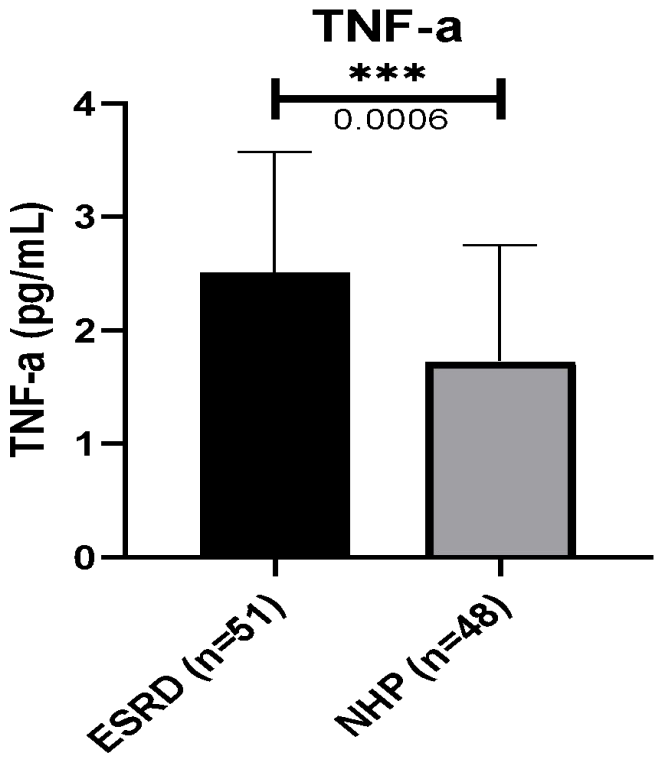


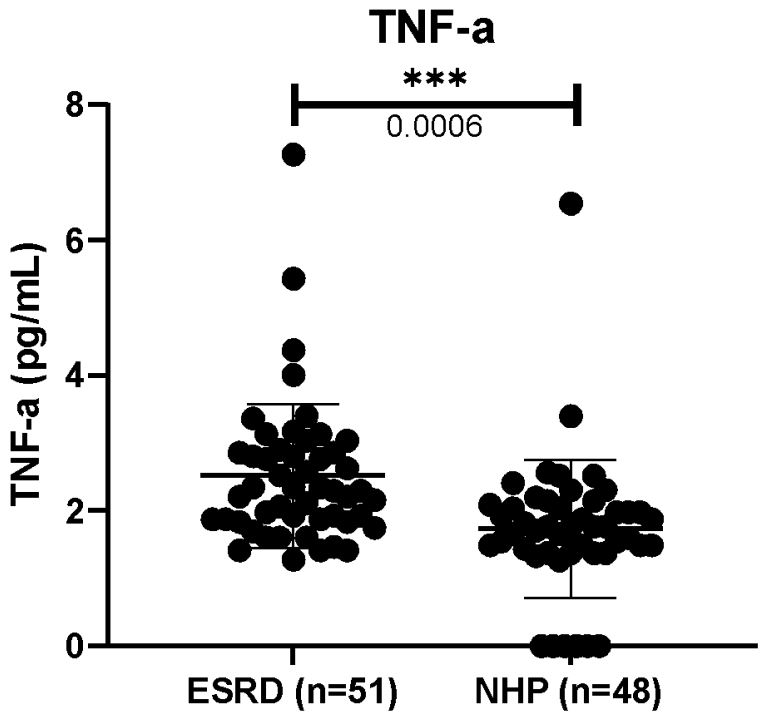
	ESRD IL-6 (pg/mL)	NHP IL-6 (pg/mL)
Average	5.2114	1.24854167
SD	10.35810104	1.23692135
SEM	1.4649	0.1786
Min	0.51	0.25
Max	73.99	7.29

% Change of Mean	317.413%

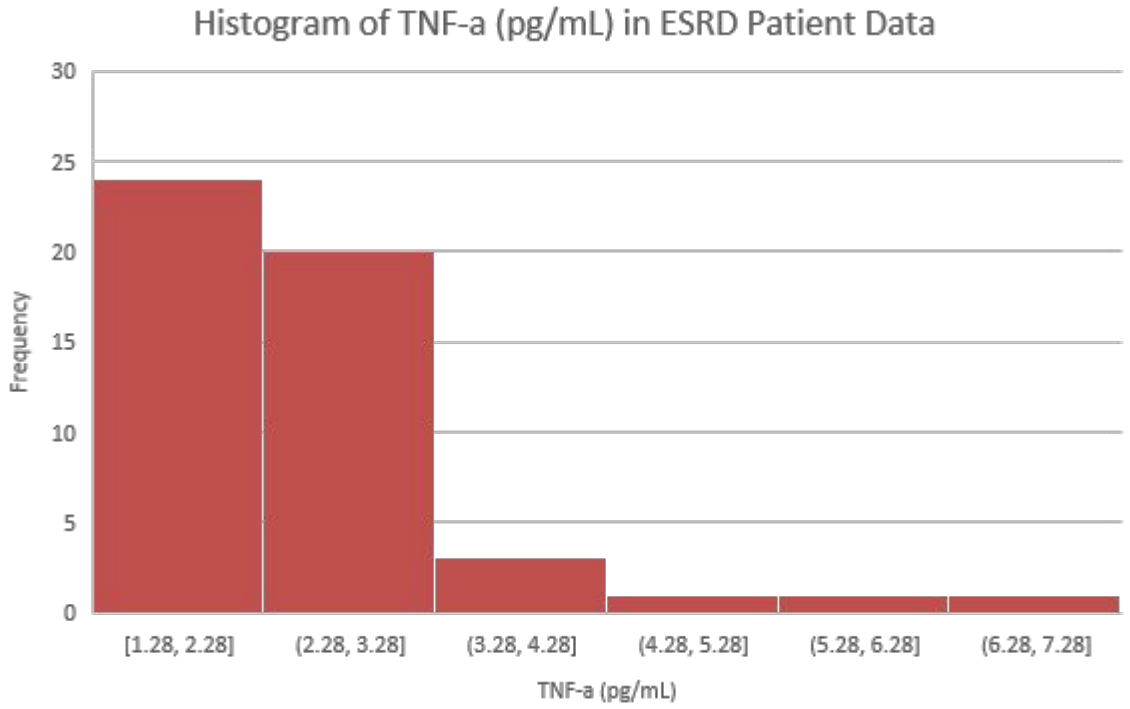
- Skewness = 1.649

TNF-A DATA ANALYSIS





TNF-A DATA ANALYSIS

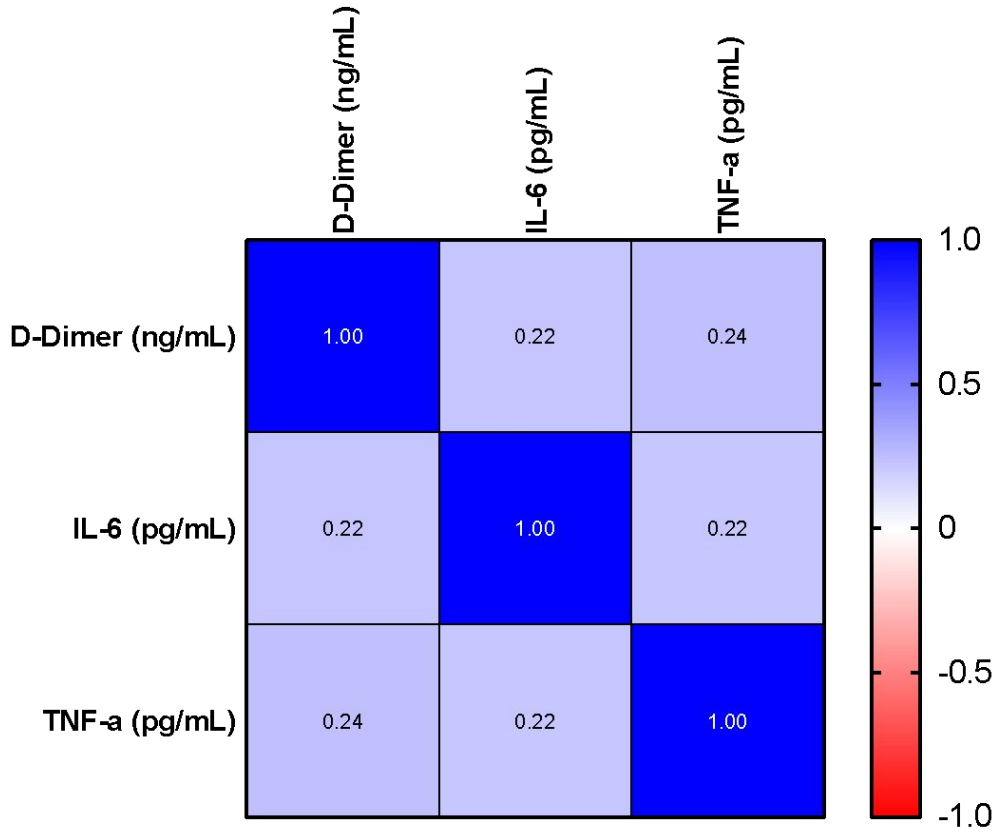


	ESRD Data (pg/mL)	Control Data (pg/mL)
Average	2.515	1.73
SD	1.06	1.026
SEM	0.148	0.148
Min	1.28	0
Max	7.27	6.55

% Change of Mean	45.376%

- Skewness = 2.402

CORRELATION ANALYSIS



CONCLUSION

- Subjects with ESRD had higher levels of D-dimer, IL-6, and TNF-α, likely due to these biomarkers' relation to inflammation and kidney dysfunction.
- The levels of thrombo-inflammatory biomarkers (D-dimer, IL-6, and TNF-α) in ESRD patients show statistically significant elevation.
- Outliers did not affect overall conclusion made of the data.
- Upregulation of these three biomarkers could be an indication of ESRD.

FUTURE PLANS

- More research can be done using greater sample sizes to determine if a potential future diagnosis of patients with ESRD can be done using thrombo-inflammatory biomarkers.
- Abstract will be submitted for Experimental Biology meeting and publication.

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Thank You

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