Salivary and Urinary Metabolomics Study in Immunoglobulin A Nephropathy Patients

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INTRODUCTION

Immunoglobulin A nephropathy (IgAN) is the most common form of glomerulonephritis worldwide with a strong autoimmune component. 40% of diagnosed cases end up with end stage kidney disease within 20 years from diagnosis. IgAN also affects tissues that can produce mucosal secretions such as nasopharynx and causes mucosal infections in IgAN patients. Metabolomics analysis allows us to analyze the differentiation in metabolite levels in biofluids like urine and serum. We aimed to evaluate the disease from a different perspective including saliva and assess the metabolomic differences between healthy people and IgAN patients and evaluate the correlation between urinary and salivary metabolomics in IgAN patients.

METHODOLOGY

This study is based on two groups as healthy control and IgAN patients groups. 16 IgAN patients were selected from patients with already have a biopsy proven diagnosis or patients that got diagnosed during ongoing research time in Bezmialem Vakif University Medical School Hospital. Patients on immunosuppressive treatment, patients with systemic diseases such as systemic lupus erythematosus, AIDS, cystic fibrosis, Sjögren's syndrome etc.; patients with active tooth decays, unhealthy periodontal tissues, removable denture, dental splints, ongoing orthodontic treatment; patients who use anti acne meds, antipsychotics, antidepressants; patients who are pregnant and patients who has used antibiotics in the last 6 months were excluded. 13 healthy control patients were chosen from healthy volunteers who fit the exclusion criterias. Stimulated salivary samples and spot urine samples were collected from both groups and preserved in -80 centigrade freezer. Collected samples were put to two stepped phase separation process and then they were put to full metabolome analysis in Liquid Chromatography-Mass Spectrometry (LC-MS/MS) device. Also general demographic information of subjects (age, height, weight etc.), serum urea, serum creatinine, urine creatinine, urine proteinuria, eGFR levels of subjects were gathered for the statistical analysis.

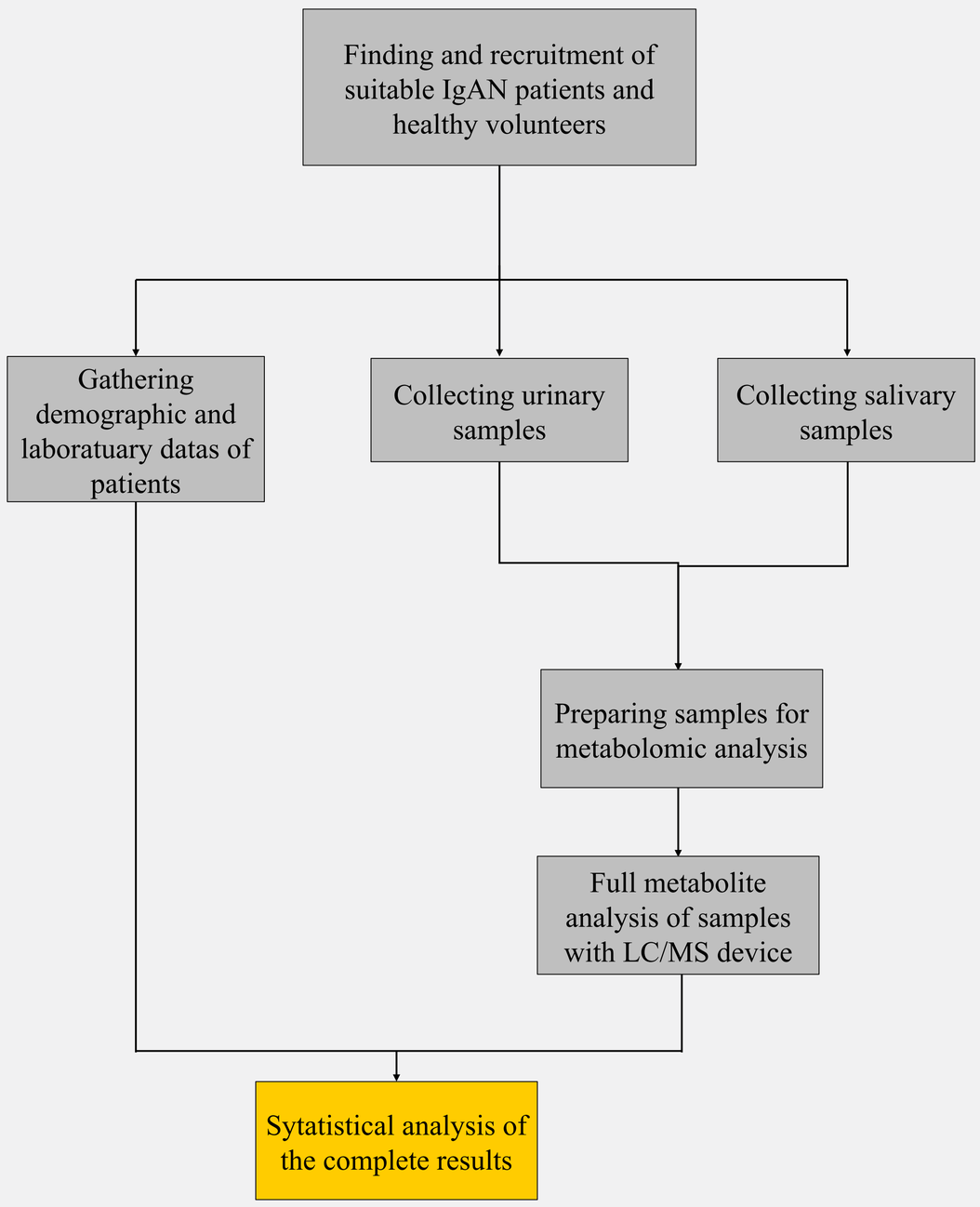

Figure 1. Demonstration of the methodology

RESULTS

Sixteen IgAN patients participated in the study. 4 of 16 patients were male and the mean age of the IgAN group was 45.31±6.651 years. Thirteen healthy controls participated in the study. 5 of 13 controls were male and the mean age of the healthy control group was 41.46±6.009 years.

When the supplementary data in Table 1 was evaluated there was no significant difference in age, height, weight and body mass index between IgAN patients and healthy controls.

Table 1. Mean and median values of participant's demographic datas

	IgAN Patients (n=16)	Healthy Control (n=13)	*p Value*
Age (years)	45,31±6,651	41,46±6,009	*0,117*
	47 (32-55)	42 (29-53)	
Height (cm)	163,63±9,885	166,46±9,938	*0,450*
	163 (145-183)	165 (152-184)	
Weight (kg)	77,88±9,979	76,92±9,878	*0,799*
	79,50 (53-90)	76 (59-98)	
Body Mass Index (kg/m²)	29,1639±3,59784	27,7871±2,97970	*0,279*
	28,9234 (19,95-34,48)	29,2969 (23,81-31,99)	

When the supplementary data in Table 2 was evaluated the IgAN patients had meaningfully increased serum creatinine and urine proteinuria levels as compared to the healthy controls (p=0.019 and p=0.002). And GFR levels were found meaningfully decreased in IgAN patients (p=0.007). However there were no significant differences on the age, height, weight, body mass index, serum urea and urine creatinine levels between the two groups (in order p=0.117; p=0.450; p=0.799; p=0.279; p=0,475 and p=0,113).

Table 2. Mean and median values of participant's laboratory findings of their kidney function tests.

	IgAN Patients (n=16)	Healthy Control (n=13)	*p Value*
Serum Urea (mg/dL)	41,6669±25,69364	30,3077±7,36415	*0,475*
	29,9450 (24-107)	32,0 (17-43)	
Serum Creatinine (mg/dL)	1,0413±0,31578	0,8038±0,14517	*0,019*
	1,0050 (0,55-1,63)	0,82 (0,59-0,99)	
Urine Creatinine (mg/dL)	89,1913±31,57473	110,9215±39,82042	*0,113*
	83,4550 (31,79-149,10)	93,960 (48,31-178,07)	
Urine Proteinuria (mg/dL)	328,6013±650,14941	14,7385±6,28312	*0,002*
	33,0 (6,50-2370,00)	13,70 (7,30-26,00)	
eGFR ml/min/1.73 m2)	75,19±24,536	98,31±16,007	*0,007*
	70,50 (35-122)	102,00 (71-121)	

CONCULUSION & DISCUSSION

Due to our challenging exclusion criterias and time limitations we were able to found lower numbers of participants than expected for both groups. Even though the participant numbers are low, we can see the meaningful changes in participant's kidney function tests between the two groups. We put the samples through full metabolomic analysis in LC-MS/MS device and currently we are analysing the results of metabolomic analysis. Further systatical analysis of the metabolomic profiles will be done.

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