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IMPACTS OF HIGH LEVELS OF SERUM LEPTIN ON THROMBOCYTE ACCUMULATION IN KIDNEY PATIENTS

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Abstract:

Objective: *The level of serum leptin was very high in the patients suffering from kidney diseases in accordance with normal healthy population. The aim of this study is to interrogate the impacts of the levels of serum leptin on thrombocyte accumulation in the patients under dialysis.*

Methodology: *Total 43 patients under peritoneal dialysis were the part of this research work. The calculation of the thrombocyte accumulation carried out from complete blood, consequently the investigation of the impacts of various concentrations of recombinant leptin in human on the TA (Thrombocyte Aggregations) carried out. There was the utilization of 4 test cells. There was no addition of the leptin in the 1st test cell, rising leptin amount was increasing in 2nd, 3rd and 4rth cells to obtain the concentrations of 25 ng/ml, 50 ng/ml & 100 ng/ml correspondingly.*

Results: *There was inhibition TA in recombinant leptin in the patients under dialysis. The average amounts of TA were very high in the 1st test cell when compared with the groups of leptin in the patients under peritoneal dialysis. We were unable to find out the significant disparity for average values of TA among every group.*

Conclusion: *Future research works with high amount of the patients under peritoneal dialysis are the requirement to give the evidence of leptin on TA.*

Keywords: *Membrane, Recombinant, Leptin, Serum, Dialysis, Accumulation, Thrombocyte.*

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INTRODUCTION:

CVDs (Cardiovascular Diseases) & their unfavorable incidences are the main reason of mortality & morbidity in among the patients suffering from kidney diseases [1]. There is importance of athero-thrombosis aggregation of platelets & adhesion in their development [2]. Leptin is a hormone of 16 kDa protein created from the adipocytes. The receptor (OBR) of its cell membrane belongs to the Class-1 family of the cytokine receptors [3]. After discovery of the OBR in the cell line of mega-karyoblastic, the association between leptin & function of the platelet was under investigation [4]. OBR-b which is very long form of OBR is detectable on the membrane of platelets [4, 5]. The research work carried out on healthy persons with administration of in vitro leptin showed different outcomes on the platelets aggregation which is a result of activation from agonist. Whereas some research works found with the view that leptin is the cause of increase in aggregation of platelet [4-7]. One research work concluded no impact [8]. The level of the serum leptin is high in the patients suffering from kidney failure which is ancillary to inflammation, less glomerular rate of filtration and high resistance to insulin [9]. M.P. Fontan in his research work found that high level of serum leptin in the patients under peritoneal dialysis in comparison with the patients under hemodialysis & pre-dialysis stage five of chronic kidney diseases [10].

METHODOLOGY:

Total 43 patients were the part of this research work. The duration of this study was from November 2018 to May 2019 in department of nephrology of Mayo Hospital Lahore. The selection of these patients carried out randomly. At least three-month duration of peritoneal dialysis, written willing from patients and age from eighteen to eighty years was the inclusion standard of this research study. All the patients were victims of diabetes, defects of platelet adhesion like disease of Willebrand, syndrome of Bernard-Soulier or defect of aggregation of platelets like Glanzmann's thrombasthenia; previous history of infection in past ten days and use of the medicines in those days as ticlopidine, acetylsalicylic acid, and beta lactam antibiotics. Ethical committee of the hospital gave the approval for the conduction of this research work. All the participants gave consent to participate this research work.

The collection of the samples of blood from all patients carried out after fasting of eight hours. The determination of the level of serum leptin carried out with the help of ELISA procedure. The addition of the solution of ADP to test cells carried out to obtain the final concentration of ten 10 µmole/L. MEA (Multiple Electrode Platelet Aggregometr) was in use for the evaluation of the function of thrombocyte. Three calculations of aggregation, velocity and area under the curve (AUC) which is the best marker of the aggregation of platelets. The preparation of 4 test cells for each patient carried out and the process on each cell carried out in sequence.

ADP put into the first cell C1 and measurement of the aggregation of platelets carried out. For every remaining test cells, in addition to first cell C1's content, rising quantity of solution of serum leptin added in sequence and measurement of the aggregation of platelets carried out. Aggregation time graph which was in use in this research work is available in Figure-1 [11]. SPSS V.15 was in use for analysis of the gathered information. T test was in use for the analysis of distributed variables. The remaining variable's analysis carried out with the utilization of Mann Whitney U method. Paired T test & Wilcoxon test methods were in use for the analysis of the association among all 4 test cells. Spearman association test was in utilization to examine the association between measurements of platelet accumulation & level of serum leptin in patient and BMI of the patient.

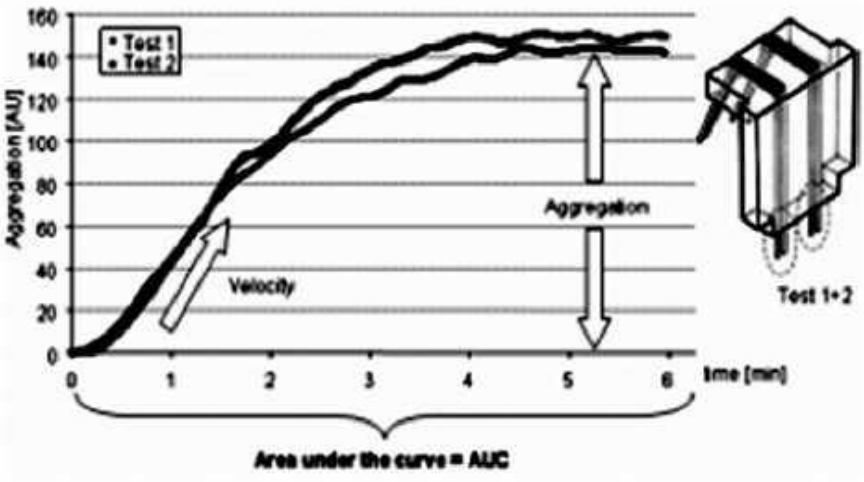


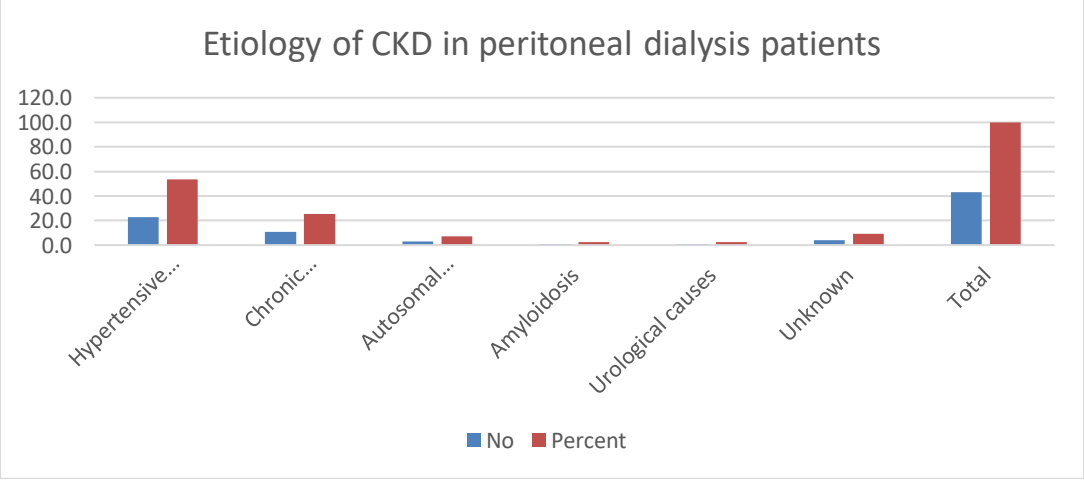
Figure 1: Aggregation –Time graph

RESULTS:

There were total forty three patients under peritoneal dialysis in which twenty one were female and twenty two were female patients. Chronic kidney diseases etiology is available in Table-1.

Table-I: Etiology of CKD in peritoneal dialysis patients.

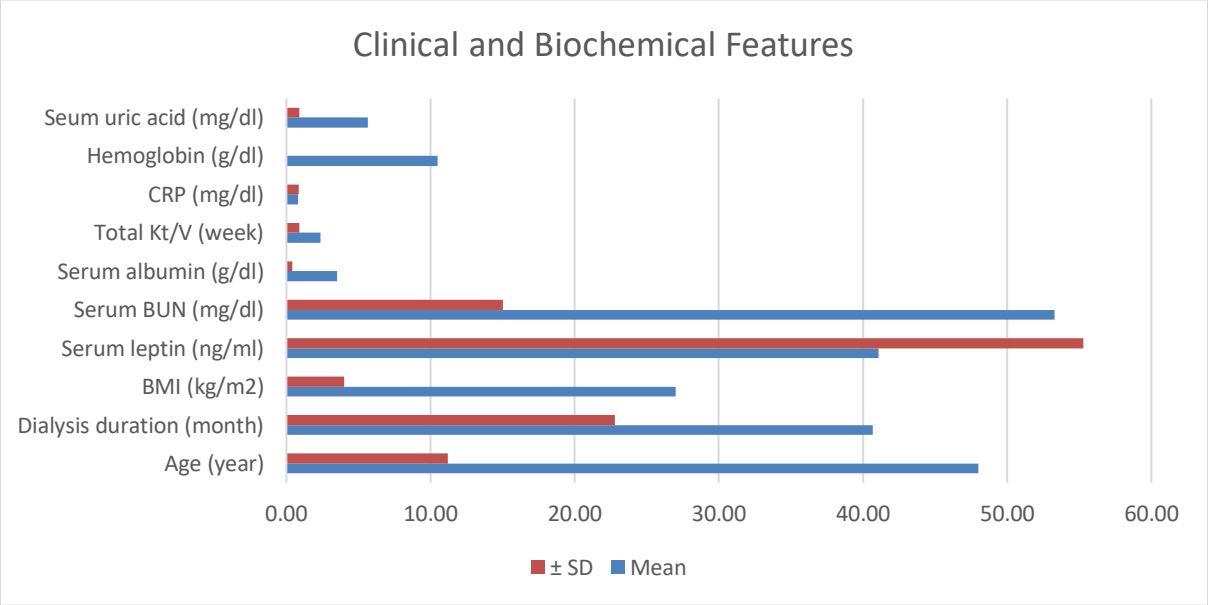
Etiology	No	Percent
Hypertensive nephropathy	23.0	53.50
Chronic glomerulonephritis	11.0	25.60
Autosomal dominant polycystic kidney disease	3.0	7.00
Amyloidosis	1.0	2.30
Urological causes	1.0	2.30
Unknown	4.0	9.30
Total	43.0	100.00



Biochemical conclusions & clinical traits of all the patients are present in Table-2. When we compared the levels of serum leptin of patients under peritoneal dialysis with the measurement of the platelets accumulation in the 1st test cell, we were unable to detect important disparity for average AUC, average value of accumulation and velocity. In the same manner, when measurements of the platelet accumulation in accordance with the results of 1st test cell compared with the mean body mass index, again no important disparity was visible among patients.

Table-II: Biochemical Findings and Clinical Characteristics of the PD Patients

Characteristics	Mean	± SD
Age (year)	48.00	11.20
Dialysis duration (month)	40.70	22.80
BMI (kg/m^2)	27.00	4.00
Serum leptin (ng/ml)	41.10	55.30
Serum BUN (mg/dl)	53.30	15.00
Serum albumin (g/dl)	3.50	0.40
Total Kt/V (week)	2.37	0.90
CRP (mg/dl)	0.81	0.86
PLT (mm^3)	254332.00	72779.00
WBC (mm3)	7112.00	1779.00
Hemoglobin (g/dl)	10.50	`.9
Seum uric acid (mg/dl)	5.65	0.90
Serum parathormone (µg/ml)	568.40	637.60
Ferritin (ng/ml)	604.60	494.80



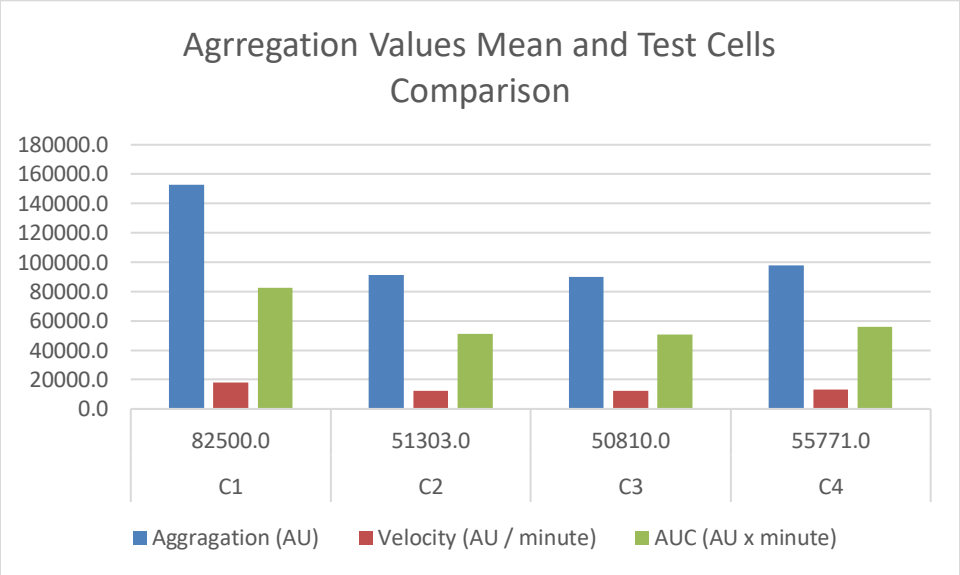
The average values of platelets accumulation of the patients and comparisons of all the available test cells are present in Table-3. P value of first cell with 2nd, 3rd and 4th for AUC and average values of aggregation were .001, and P values of value of average velocity were available as .016, .004 & .001 for the similar comparison of the test cells correspondingly. For the group of serum leptin, we

were unable to find any significant disparity for AUC, average velocity and average values of aggregation between the groups. When we separated the patients of PD in accordance to their levels of the serum leptin calculated in current year as those greater (16) and under (27) in levels measured in the recent year twenty five ng/ml

In both groups and we carried out comparison of the parameters of their aggregation with the first test cell but we were still unable to find the high aggregation of platelets in the group with high level of serum leptin.

Table-III: The mean platelet aggregation values of PD patients and comparison of test cells.

Mean value	C1	C2	C3	C4
AUC (AU x minute)	82500.0	51303.0	50810.0	55771.0
Aggragation (AU)	152713.0	91194.0	90034.0	97882.0
Velocity (AU / minute)	17832.0	12416.0	12483.0	13386.0



DISCUSSION:

In this research work, the measurement of the aggregation of platelets carried out with the help of Multi-plate device which has the ability to measure the complete blood. In various research works measuring the impact of leptin on the aggregation of platelets, authors gave preference to the use of plasma rich with platelet [4-8]. The samples of blood gave a provision of high physiological atmosphere for aggregation of platelets than the other procedures since elements with other shaped together with platelets are available in the complete blood [12]. Neutrophils & monocytes form heterotypic accumulates together with platelets via molecules of p-selectin available on the upper surface of platelets & leukocytes [13].

The interaction of platelet-neutrophil in the complete blood particularly in initial stage ay reduce the response of platelets [14]. This method is not easily understandable, the relation of platelets with the erythrocytes enhances the effectiveness and their operational ability [15]. Malyszko in his research work interrogating the association between plasma & levels of leptin in the peritoneal fluid with the aggregation of the platelets with the use of the ristocetin & arachidonic acid as the major agonists, discovered a strong association among these features [16]. We were not able to determine a significant disparity among the aggregation of platelets with various concentrations of serum leptin.

There were some restrictions of this research work as deficiency of healthy controls, lack of the determination of serum leptin, deficiency of information about the soluble receptor of leptin and resistance of leptin. J. Beltowski concluded natriuresis & nitric oxide like impacts in his research

work on the rats for a small duration effect of serum leptin when applied precisely. In the same research work, chronically prompted hyperleptinemia was responsible for the induction of resistance to the nitric oxide and natriuresis like impacts [17]. Nitric oxide also decreases the adhesion of platelets and ability of aggregation [18].

CONCLUSION:

The platelets aggregation was very high in the patients undergoing peritoneal dialysis in this research work but the size of samples was very less. There is requirement of further case works to prove the impact of leptin on the aggregation of platelets in patients under peritoneal dialysis with a large sample size.

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