SERUM LIPID AND LIPOPROTEIN PROFILES IN CHILDREN WITH GLOMERULAR DISEASES AT THE KENYATTA NATIONAL HOSPITAL.

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A dissertation presented in part fulfilment for the degree of Masters of Medicine (Paediatrics) of the University of Nairobi.

by

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1988

D E D I C A T I O N

To my mother CONSTANCE NAIGA NALONGO who inspired me to join the medical profession

D E C L A R A T I O N.

I certify that this thesis is my own original work and has not been presented for a degree in any University

Signed .....

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LIST OF ABBREVIATIONS

ARF	-	Acute renal failure
BP	-	Blood Pressure
BUN	-	Blood Urea and Nitrogen
BCG	-	Bromocresol-green
CRF	-	Chronic renal failure
CAD	-	Coronary Artery Disease
CHD	-	Coronary Heart Disease
DPGN	-	Diffuse Proliferative glomerulo Nephritis
ESRD	-	End Stage Renal Disease
FGS	-	Focal glomeruloclerosis
Gm/L	-	Grams/litres
HB	-	Heamoglobin
HDL	-	High Density Lipoprotein
HT	-	Hypertension
ISKDC	-	International Study on Kidney Diseases in Children
IVU	-	Intravenous Urogram
IHD	-	Ischaemic heart disease
KNH	-	Kenyatta National Hospital
LDL	-	Low density lipoprotein
Umol/l	-	Micromoles/litres
MCGN	-	Minimal change glomerulo nephritis
K^+	-	Potassium ion
QMN	-	Quartan Malaira nephropathy
r.p.m.	-	Revolutions per minute
Na^+	-	Sodium ion
SLE	-	Systemic lupus erythromatosus
TC	-	Total cholesterol
VLDL	-	Very low density lipoprotein

SUMMARY

The fasting serum lipid and lipoprotein profiles of children with glomerular diseases aged 20 years and below were studied over a nine months' period between June 1987 and Febraury, 1988 inclusive.

A total of 50 patients and 48 controls matched for age, sex and dry weight were recruited into the study. Serum electrolytes, creatinine, protein, albumin and blood urea and nitrogen were also studied. Renal biopsies were done where possible, to establish a histopathological diagnosis. A total of 44 renal biopsies were done. The renal tissue was diagonostic in 41 (82%) patients.

The majority of the patients with glomerular disease were in the 5 - 9 years age range comprising 18 (36.3%) of the study patients. There was a male predominance of 2:1. More than 25 (50%) of the patients had pure nephrosis. Hypertension and haematuria were present in 18 (36%) and 17 (34%) of the patients respectively. The controls had the following mean serum lipids and lipoporteins:-

TC 3.7 $\pm$ 0.1 mmol/L, TG 0.6 $\pm$ 0.2 mmol/L, LDL 2.5 $\pm$ 0.9 mmol/L HDL 1.02 $\pm$ 0.1 mmol/L and VLDL 0.3 $\pm$ 0.1 mmol/L. The same mean serum lipid and lipoprotein levels in the patients were as follows:- TC 7.8 $\pm$ 3.3 mmol/L TG 2.3 $\pm$ 0.9 mmol/L, LDL 5.7 $\pm$ 3.1 mmol/L, HDL 0.75 $\pm$ 0.1 mmol/L and VLDL 1.2 + 0.6 mmol/L.

Significant alterations ($P < 0.001$) in the lipid and lipoprotein profiles was found in 36/50 (72%) of the patients. These patients had elevated TC, TG, LDL and VLDL while HDL was decreased.

The patients who were being treated with corticosteroids exhibited markedly low TG and VLDL fractions. The male patients were found to have relatively higher lipid and lipoprotein fraction elevations compared to the female patients.

Focal glomerulosclerosis was the commonest histopatholigical lesion being present in 10/44 (22.7%) of all the biopsies studied. Patients with diffuse proliferative, mesangiocapillary and crescenteric histopathological lesions had the highest lipid and lipoprotein elevations.

No significant correlations were found between total serum protein both the lipid and lipoprotein fractions. Positive correlations were found between TG and BUN as well as between TG, VLDL, TC and serum albumin. Likewise a negative correlation between creatinine and TG. The mean serum lipid and lipoprotein fractions observed in the study patients are lower than those seen in normal adults both in Kenya and in the Western world as well as those seen in Western Africa.

I N T R O D U C T I O N.

For more than a century, renal diseases have been associated with pathological hyperlipidaemia (1,2). As early as 1827, Bright (3) noted the laetescence in the sera of patients with renal diseases - Bright's diseases. Eight years later Christon attributed this to a substance that was similar to fat (2,4). It was not until 1903 that Boenniger chemically analysed this substance and found it to be lipid (5). In 1911 Chaufford and Laroche (3) reported increased serum cholesterol in patients with renal disease; and by 1929 various workers had shown that different lipid fractions were elevated to variable degrees in these patients (6-11).

In 1971, Chopra et al (12) recognised an increased incidence of ischaemic heart disease (IHD) in patients with the nephrotic syndrome. Worse still, later work has shown that the incidence of these often fatal cardiovascular diseases is occurring at an increasingly early age (6-10). Besides, atherosclerosis as sequala of hyperlipidaemia is known to begin early in life and fatty steaks in the aorta have been shown to occur in three year old children and appear in the coronaries during the second decade of life (9).

The hyperlipidaemia seen in most cases of renal diseases particularly the nephrotic syndrome is due to elevations of lipoproteins (10,12), hence the use of the term hyperlipoproteinaemia rather than hyperlipidaemia. The mechanism of hyperlipoproteinaemia in the nephrotic syndrome is complex and multifactorial. It involves a combination of reduced clearance of lipoproteins, increased hepatic synthesis of lipoproteins, reduced catabolism of lipoproteins and

albumin peripherally as well as increased urinary protein loss (albuminuria), resulting in hypoalbuminaemia (11-14). Consequently the pattern of serum lipids and lipoprotein fractions found in hyperlipoproteinaemia secondary to renal disease have tended to vary in different studies (1,3,5,11,14-17).

Both cholesterol and triglycerides are definitely known to be atherogenic and their elevation carries an increased risk of developing ischaemic heart disease (IHD), coronary heart disease (CHD) and probably hypertension (HT) (6-8, 18-21). Apart from the nephrotic syndrome, other renal diseases predispose to hyperlipoproteinaemia especially when they are associated with some degree of renal failure (1,19-21). Thus hyperlipoproteinaemia occurs with diabetic nephropathy, chronic renal failure (CRF), acute renal failure (ARF) and obstructive uropathy to mention but a few. Secondary hyperlipoproteinaemia without renal disease may result from other systemic diseases. These include systemic lupus erythematosus (SLE), diabetes mellitus and hypothyroidism. It may also result from the use of drugs such as steroids, cyclophosphamide, contraceptive pills, thiazide diuretics and alcohol.

Glomerular diseases in the tropical enviroment have been attributed to diversified aetiology. Infections and infestations undoubtedly play major aetiological roles (22-25) in the development of glomerular diseases especially the nephrotic syndrome. Thus conditions such as tuberculosis, shistosomiasis, hepatitis and malaria comprise only a few of the aetiological agents causing renal insult in the affected individuals (25).

The nature of renal damage encountered varies in different enviroments as well as with the nature of renal insult. Consequently the histopathological appearances are varied as well. They depend on the agent causing the insult.

To date, local reference values of fasting serum lipids and lipoproteins have been established in normal adult Kenyan Africans as well as in neonates (22). Thus as noted above, lipid profiles have also been established in adult Kenyan Africans with CRF by Abdallah (1) working at the Kenyatta National Hospital. These patients had markedly elevated cholesterol and triglyceride levels.

So far no work has been done to investigate the lipid profiles in children with glomerular disease. More still there has been no work to investigate the correlations among lipid profiles and histopathological lessions or the biochemical derrangements that occur in these children.

The prevalence of ischaemic heart disease in patients with glomerular diseases particularly the nephrotic syndrome, and the occurrence of this ailment in our enviroment have prompted the undertaking of this study so as to establish the lipid profile patterns that occur in these patients.

OBJECTIVES.

1. To determine the pattern of lipids and lipoprotein profiles in children with glomerular disease.

2. To determine the correlations(s) between the lipid and lipoprotein profiles with the serum BUN, creatinine, albumin and protein.

3. To investigate the relationship(s) if any between the lipid and lipoprotein profiles and the renal glomerular histopathological lesions.

MATERIALS AND METHODS.

Study Period.

A prospective cross-sectional study was conducted over nine months between June 1987 and February 1988 inclusive.

Ethical considerations.

A written consent of the Kenyatta National ethical committee and a verbal consent from the parents(s) or guardian(s) was sought and granted.

Study patients and study area.

The study was conducted at the Kenyatta National Hospital. The study patients were aged twenty years or less who were admitted to the paediatric or medical wards with an established diagnosis of glomerular disease. These patients had signs and symptoms suggestive of structural or functional renal impairment. These included: oliguria, proteinuria, oedema, azotaemia, haematuria or hypertension occuring singly or in combination. All patients admitted with established glomerular disease who satisfied the criteria listed below were entered into the study.

Exclusion Criteria.

Presence of:-

a) Systemic disease(s) associated with derranged lipid metabolism e.g diabetes mellitus, malnutrition, hypothyroidism or infections.

b) Medication known to affect lipid or lipoprotein metabolism apart from steroids or cyclophosphamide.

c) Obesity.

The details outlined in appendix 1 were elicited and recorded. The patient were categorised as having nephritic nephrosis pure nephrosis according to ISKDC criteria - appendix III.

Controls.

The controls were otherwise healthy subjects within the specified age range whose clinical condition conformed to the American standard of excellence (27,28) based on the Havard charts. Each patient had a single control matched for age, sex and dry weight. The controls were recruited from amongst patients admitted to the surgical wards for minor elective surgery such as orchidopexy, hernioraphy or contracture release

The following parameters were measured as follows:-

(i) Blood pressure

This was recorded in the suppine position on three separate occasions within a period of two weeks.

The V-LOK CUFF BAUMANOMETER Sphingimomanometer was used. Both paediatric and adult cuffs being employed depending on the age of the patient.

(ii) Height (CM).

Was measured using a calibrated wall meter, this being taken in the upright standing position.

(iii) Dry Weight

This was measured on three separate days after the oedema had subsided. The 'ACCY-WEIGH' weighing scale from metro equipment model owm 457 was used.

Laboratory methods

Following a full physical examination, the patients's biodata was recorded on proforma sheet 1 - Appendix 1. All subjects (patients and controls) were subjected to an overnight fast of at least 12 hours on the night preceeding the drawing of blood.

A. Following the overnight fast and in the absence of venous stasis, ten millilitres of whole blood was drawn from a peripheral vein using a scalp vein needle gauge number 23. The subjects lay supine while the blood was being drawn. The blood was then separated as follows:-

i) Four millilitres of blood were anticoagulated with ethylene diamine tetra acetic acid -EDTA.

ii) Six millilitres of blood were put in a plain, water washed container.

These samples were left on a bench at room temparature for about 4 hours following which they were centrifuged at 3000 r.p.m. for 10 minutes. The plasma and sera from (i) and (ii) above were separated and stored at -20 degrees centigrade till the time of analysis.

Blood analysis-

The blood analysis was done in batches.
The blood was analysed using the Technicom SMA II auto-analyser as follows:-

a) Serum-

(i) Sodium -Na^+ and potassium -K^+ using the flame photometry (29)

(ii) Creatinine by the Jaffe method (30).

(iii) Blood urea and nitrogen (BUN) after Marsh et al (31)

(iv) Albumin by the Bromocresol-Green (BCG) method (32)

(v) Total protein by the Biuret method (33).

b) Plasma

The lipid profiles were analysed using the Boehringer-Mannheim enzymatic kits as follows:-

i) Total cholesterol by the CHOD-PAP enzymatic calorimetric method (34)

ii) Triglyceride after Wahlefeld (35)

iii) High density lipoprotein-cholesterol by the precipitation method (36).

iv) The very low density lipoprotein cholesterol (VLDL) and low density lipoprotein (LDL) were calculated using the Friedwald equation (37) as follows:-

1. $LDL = TC - (\frac{TG}{2.2} + HDL)$

and

2. $VLDL = TC - (LDL + HDL)$

Where

LDL = Low density lipoprotein

TC = Total cholesterol

TG = Triglyceride

VLDL = Very low density lipoprotein

HDL = High density lipoprotein

B. Renal Biopsy

The patients who were deemed clinically fit to withstand the procedure had a percuteneous renal biopsy done on them under ultrasound guidance. The Kidney size and depth were established by ultrasound. The biopsies were done using the Tru-cut Travenol^{R} biopsy needles. For patients aged 15 years or less, the biopsies were done under general anaesthesia while in those older than 15 years, they were done under local anaethetic.

Preoperatively, the patients selected for renal biopsy had the following normal parameters:-

- Intravenous urogram (IVU)
- Prothrombin Index > 75%
- Haemoglobin (Hb) > 10gm/dl
- Normal sized kidneys as seen on ultrasonography
- Absolute platelet count > 150,000/mm^3

Forty four of the fifty patients recruited had renal biopsies done on them.

C. Urine.

A mid stream urine (msu) specimen was collected from each patient and was analysed as follows:-

i) Microscopy:

Microscopy of the centrifuged urine deposit was done and the following sought:-

- Red blood cells
- Red blood cell casts
- Bacteria

ii) Biochemistry:

Using a Combur-Test^{R} - Boehringer-Mannheim, Urinary protein estimates were made as follows:-

Absent	- Nil/trace	< 30 mg/dl
Mild	(+)	> 30 mg/dl
Moderate	(++)	>100 mg/dl
severe	(+++)	>500 mg/dl

The results of all the above analyses were recorded on proforma sheet II-Appendix II.

The results obtained were then subjected to statistical analysis using the students t-test and linear regression.

RESULTS

Patients and control data

During the study period, a total of fifty consecutive patients with established glomerular disease who conformed to the inclusion criteria were recruited into the study. Their age and sex distribution are illustrated in Tabel 1. The overall male to female ratio was approximately 2:1. The peak age range was 5-9 years comprising 36.3% of the study Population. There were forty eight controls recruited into the study. Their age and sex distribution are also illustrated in Table I.

Table 2 illustrates the clinical diagnosis by age group. Twenty-six patients had the pure nephrosis picture, comprising 52% of the study population. Twenty-four patients making up 48% had nephritic nephrosis. There were 4 patients (8%) with CRF who also had features of nephritic nephrosis. The physical features observed in the study patients are illustrated in Table 3. Proteinuria and oedema were the most frequent features comprising 92% and 78% respectively. Hypertension was present in 36% of the patients while haematuria occurred in 28% of patients. Spleenomegaly and hepatomegaly were found in 18% and 16% of the patients respectively. They occurred mainly in patients from malarious areas.

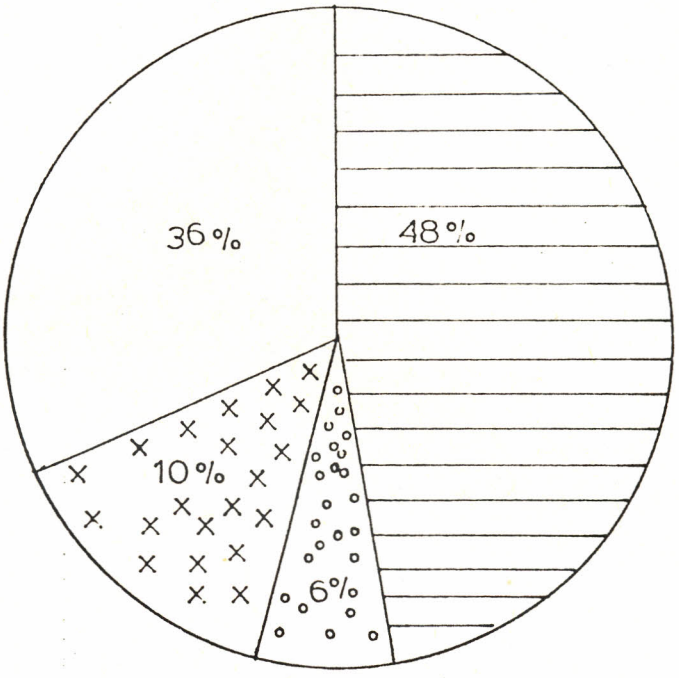
Figure I illustrates the estimated degree of proteinuria in the study population. Upto 84% had moderate to severe proteinuria i.e >100 mg/dl. The majority,48% had severe proteinuria (>500 mg/dl).

Table 1: Age and sex distribution of patients and controls.

	patients (n=50)		Controls (n=48)		%
Age range in years	Males	Females	Males	Females	
0 - 4	4	2	4	2	13.7
5 - 9	13	5	12	5	36.3
10-14	8	4	8	4	25
15-19	7	7	7	6	25
Total	32	18	31	17	100

Table 2: Patients' distribution by clinical diagnosis and age.

Diagnosis / Age range in years	Pure nephrosis	Nephritic nephrosis
0 - 4	4 (66.7%)	2 (33.3%)
5 - 9	11 (58%)	7 (37%)
10 - 14	5 (42%)	7 (58%)
15- 19	6 (43%)	8 (57%)
Total	26 (52%)	24 (48%)



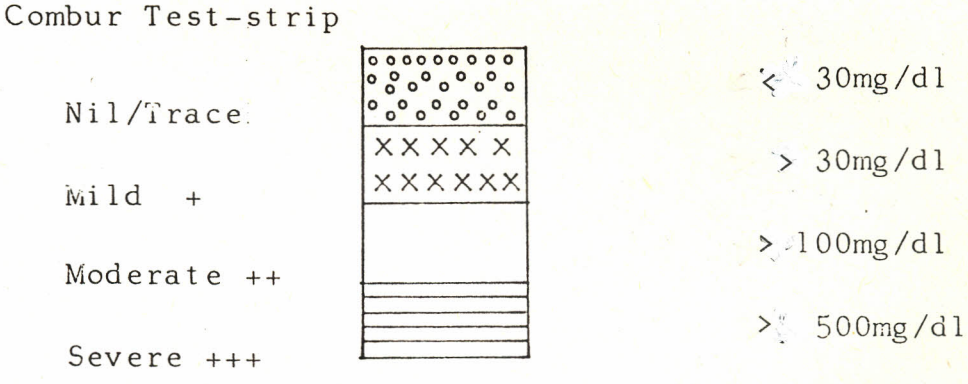


Figure 1: Patient's degree of proteinuria.

Table 3: Patients' physical features.

Physical features	Number of patients	%
1. Oedema	39	78
2. Ascites/anarsarca	31	62
3. Hypertension*	18	36
4. Haematuria	17	34
5. Protenuria	46	92
6. Splenomegaly	9	18
7. Hepatomegaly	8	16

*Hypertension was considered present if the blood pressure (BP) exceed:-

age in years	BP (mmHg)
<6 years	110/70
6 - 9 Yrs	120/75
10-14 "	130/80
14-19 "	140/85

or if the patients were on anti-hypertensive drugs.(62)*

*( ) Reference.

Biopsy data

Renal biopsies were done on 44/50 patients comprising 88% of all study patients. The biopsies were diagnostic in (41/44) 93.2% cases. Inadequate renal tissue was obtained in (3/44) 7.3% patients.The observed histopathological lesions are illustrated in Table 4. Focal glomerulosclerosis (FGS) was the most frequent lesion seen, comprising 22.7% of all biopsies done. It was followed by mesangiocapillary glomerulonephritis and 15.9% mesangioproliferative glomerulonephritis 11.4%, diffuse proliferative glomerulonephritis and end stage renal disease each comprising 9.2%. Membranous nephropathy occured in 6.8%. Tuberculous nephropathy was observed in a single patient 2.2% and so was malaria nephropathy. Inadequate biopsy tissue is shown as unclassified histopathology comprising 6.8%.

Biochemical Data.

Table 5 illustrates the mean serum biochemical parameters as well as the lipid profiles in both the patients and the controls. From this table it is evident that the patients were relatively hyponatraemic. This can be attributed to the inherent fluid retention and therefore haemodilution.

The potassium levels were not different in the two groups. As expected both the BUN and creatinine levels were elevated in the patients as compared to the controls. Serum proteins as well as albumin were diminished in the patients. It is quite evident that marked differences occurred in the lipid profiles between the patients and the controls. All lipid fractions apart from HDL were higher in the patients than the controls.

Table 4: Distribution of histopathological lesions.

Histopathological lesion	Number of patients n=44	%
1. Minimal lesion glomerulonephritis(MCGN)	0	0
2. Focal segmental glomerulonephritis with sclerosis (FGS)	10	22.7
3. Mesangiocapillary glomerulonephritis (MCGN).	7	15.9
4. Mesangial proliferative glomerulonephritis(MPGN)	6	13.6
5. Crescenteric glomerulonephritis(crescenteric)	5	11.4
6. Diffuse proliferative glomerulonephritis(DPGN)	4	9.2
7. End stage renal disease (ESRD)	4	9.2
8. Membrananous nephropathy	3	6.8
9. Unclassified*	3	6.8
10. Malaria nephropathy(QMN)	1	2.2
11. Tuberculous nephritis	1	2.2
	44	100

*These had inadequate renal tissue for diagnosis.

Table 5: Mean serum levels of biochemical parameters for patients and controls.

	Patients	Controls	P-value
Sodium (mmol/l)	132±5.3	140.6±3.6	<0.01 S
Potassium (mmol/l)	4.5±0.6	4.4±0.4	- NS
BUN (mmol/l)	10.3±9.0	4.1±1.1	0.001 S
Creatinine (Umol/l)	207±3.0	104+80	<0.01 S
Protein (gm/l)	54.5±12.4	71.6+6.8	<0.1 NS
Albumin (gm/l)	24.4±7.5	39.5+4.2	<0.001 S
Total cholesterol (mmol/l)	7.8±3.3	3.7±0.9	<0.001 S
Triglycerides (mmol/l)	2.3±0.9	0.6±0.2	<0.001 S
LDL (mmol/l)	5.7±3.1	2.5±0.9	<0.001 S
HDL (mmol/l)	0.75±0.1	1.02±0.1	<0.001 S
VLDL (mmol/l)	1.2±0.6	0.3±0.1	<0.001 S

S = Significant
NS = Not significant

Table 6 illustrates the lipid and lipoprotein ranges in normal controls by age and sex. The females had a higher lower limit while the males had a higher upper limit of total cholesterol i.e 2.1 mmoles/l and 6.3 mmoles/l respectively. With triglycerides, both sexes had the same lower limit but the upper limits were 0.8mmoles/l for females and 1.2mmoles/l for males. The picture for LDL and VLDL were not very different in the two groups. HDL was the same for both sexes.

Table 7. compares the lipid profiles of normal subjects between adults in different enviroments and the children in our study at Kenyatta National Hospital. The lipid fractions were higher in adult caucasian population and lowest in the Kenyan African children. Adult african kenya subjects on the other hand had lipid fraction levels that were intermediate between those of the other two groups.

Table 6: Lipid and lipoprotein ranges in normal controls by sex.

Lipid / Sex	TC	TG	LDL	VLDL	HDL
Males	2.1-6.3	0.5-1.2	1.0-4.8	0.2-0.9	0.7-1.2
Females	2.8-4.8	0.5-0.8	1.5-3.7	0.2-0.5	0.7-1.2
All controls	2.5-5.7	0.5-1.2	1.0-4.8	0.2-0.9	0.7-1.2

	ADULTS				CHILDREN	
	Ojwang et al (22)**		Short et al (57)*		This study	
	Male	Female	Male	Female	Male	Female
TG	0.83±0.36	0.66±0.39	1.78±0.03	1.42±0.12	0.65±0.2	0.64±0.1
TC	4.73±0.7	4.46±0.76	7.46±0.66	7.22±0.86	3.6±0.9	3.8±0.65
LDL	3.3±0.72	2.89±0.71	5.09±0.58	4.97±0.71	2.3±0.8	2.5±0.64
VLDL	0.39±0.19	0.30±0.17	0.94±0.32	0.50±0.13	0.34±0.1	0.31±0.1
HDL	1.04±0.34	1.18±0.25	1.35±0.09	1.55±0.24	1.02±0.12	1.02±0.15

Table 7: Comparison of normal controls' mean lipid fractions in the study with other studies.

( )* References.

Overall, lipid and lipoprotein levels were higher in the males than in the females. Hyperlipidaemia occured in 36/50 (72%) of the patients.

Tables 8a and 8b illustrate patient's and control's mean serum lipid by age group. They show markedly elevated levels in patients as compared with the controls. The lipid levels were generally higher in the 0-4 years age group for both patients and controls. The HDL fraction was lower in all patients. A two to three fold increase is noticeable in TC between controls and patients.

Figure 2 illustrates the lipid fractions between the patients and controls. All lipid fractions were elevated in the patients as compared with the controls except for the HDL which was reduced.

Tables 9a and 9b illustrate patient's mean serum lipids by age and sex. The lipids were higher in the males than in the females. There was no difference in both VLDL and HDL in the 10-14 years age group.

Figure 3 illustrates the mean serum TC of both the male and female patients. TC were higher in the males in all age groups except in the age group 5-9 years where it was higher in the females.

Table 10 compares the mean serum lipids in patients treated with corticosteroids with those who were not treated with corticosteroids. There were 12/50 (24%) patients treated with corticosteroids. The corticosteroids treated patients had relatively lower lipid fraction elevations particularly TG and VLDL. LDL was slightly higher in the corticosteroid treated patients. HDL was not affected by corticosteroid therapy.

Table 8a: Patients and controls mean serum lipids by age (0 - 9 Yrs)

Age Range Years	Lipid	TC	TG	LDL	VLDL	HDL
0-4	Patient	6.6±1.5	2.3±0.8	3.5±1.8	2.1±0.5	0.72±0.2
	Control	4.8±1.5	0.9±0.2	3.4±0.9	0.4±0.1	0.98±0.13
	P-Value	<0.01	>0.5	<0.01	<0.001	<0.01
5-9	Patient	7.5±3.2	2.0±1.0	5.5±2.6	1.0±0.5	0.74±0.1
	Control	4.1±0.5	0.6±0.1	2.7±0.4	0.3±0.1	1.18±0.15
	P-Value	<0.001	<0.001	<0.001	<0.001	<0.001

Table 8b: Patients and controls mean serum lipids by age (10-19yrs)

Age Range in Years	Lipid	TC	TG	LDL	VLDL	HDL
10 - 14	Patients	9.2±4.1	2.8±0.9	7.1±3.6	1.18±0.53	0.68±0.16
	Controls	3.5±0.8	0.6±0.1	2.2±0.8	0.29±0.14	1.0±0.14
	P-value	<0.001	<0.001	<0.001	<0.001	<0.001
15 - 19	Patients	7.7±3.3	2.2±0.8	5.8±3.2	1.16±0.3	0.74±0.14
	Controls	3.3±0.6	0.6±0.1	1.1±0.1	0.28±0.04	1.0±0.12
	P-value	<0.001	<0.001	<0.001	<0.001	<0.001

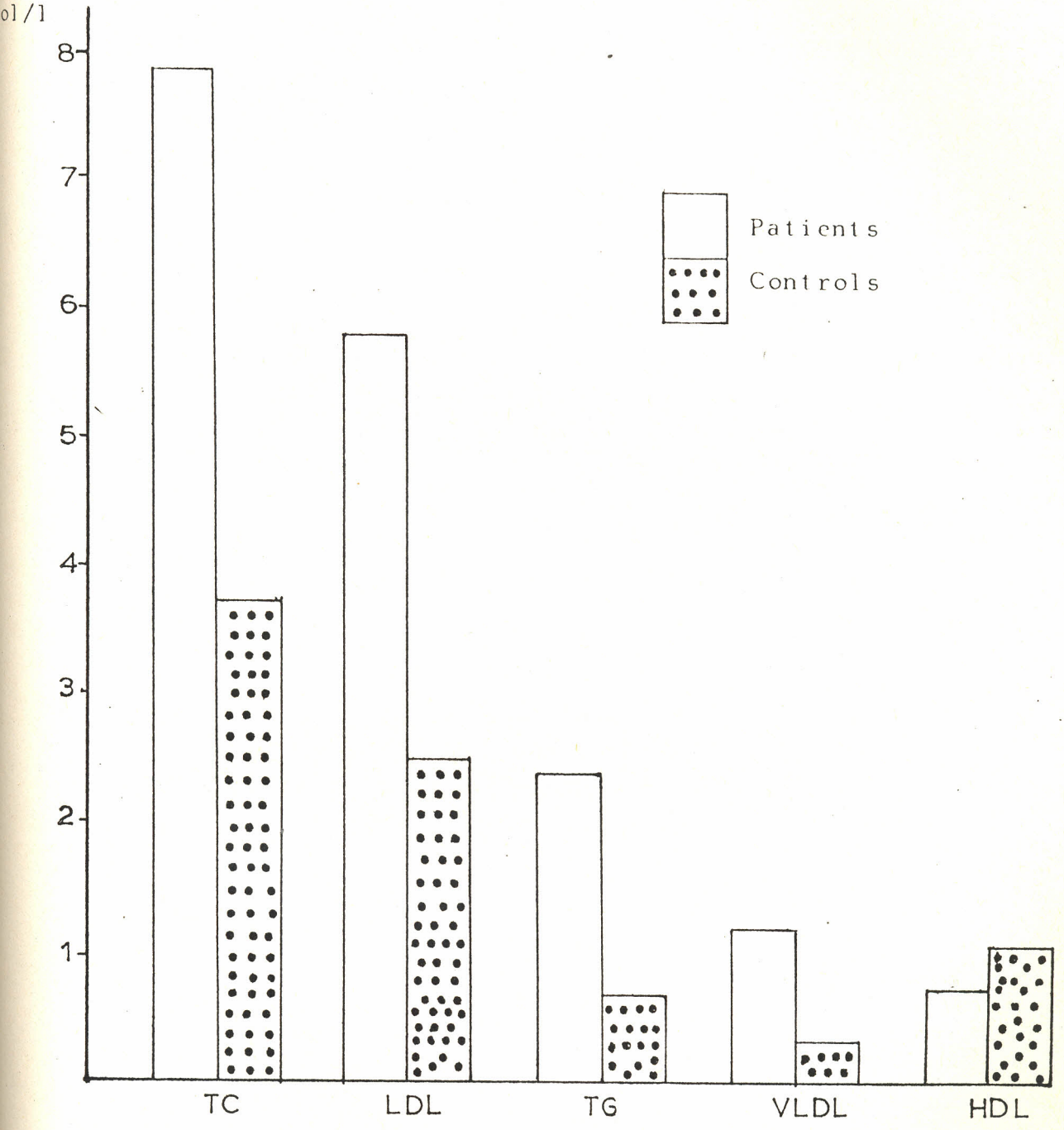


Figure 2: Patients' and controls' mean serum lipids.

Table 9a: Patients mean lipids distribution by age and sex (0-9Yrs)

Age Range in Years	Lipid Sex	TC	TG	LDL	VLDL	HDL
0 - 4	Male	7.1±1.9	2.4±0.9	12.7±2.6	2.0±0.1	0.8±0.2
	Female	5.9±0.2	2.1±0.1	2.5±0.3	2.5±0.3	0.63±0.1
	P-value	<0.001 S	<0.001 S	<0.001 S	<0.00 S	<0.001 S
5 - 9	Male	6.8±2.4	1.9±0.7	5.3±2.1	0.9±0.3	0.8±0.1
	Female	9.7±4.8	2.5±1.8	7.5±4.0	1.3±0.8	0.6±0.1
	P-value	<0.001 S	<0.001 S	<0.001 S	<0.001 S	<0.001 S

S = Significant

Table 9b: Patients mean lipids distribution by age and sex (10-19Yrs)

Age Range in Years	Lipid / Sex	TC	TG	LDL	VLDL	HDL
10-14	Males	10.3±3.7	2.9±1.0	8.1±3.2	1.2±0.6	0.7±0.2
	Females	6.9±4.3	2.4±1.0	5.1±3.9	1.2±0.4	0.7±0.1
	P-value	<0.001	<0.001	<0.001	-	-
15-19	Males	7.9±2.3	2.4±0.7	6.1±2.1	1.3±0.3	0.7±0.1
	Females	7.5±4.0	2.0±0.9	5.6±2.4	1.1±0.4	0.8±0.4
	P-value	<0.001	<0.001	<0.001	<0.001	<0.001

Figure 3: Patients mean serum TC by age group and sex

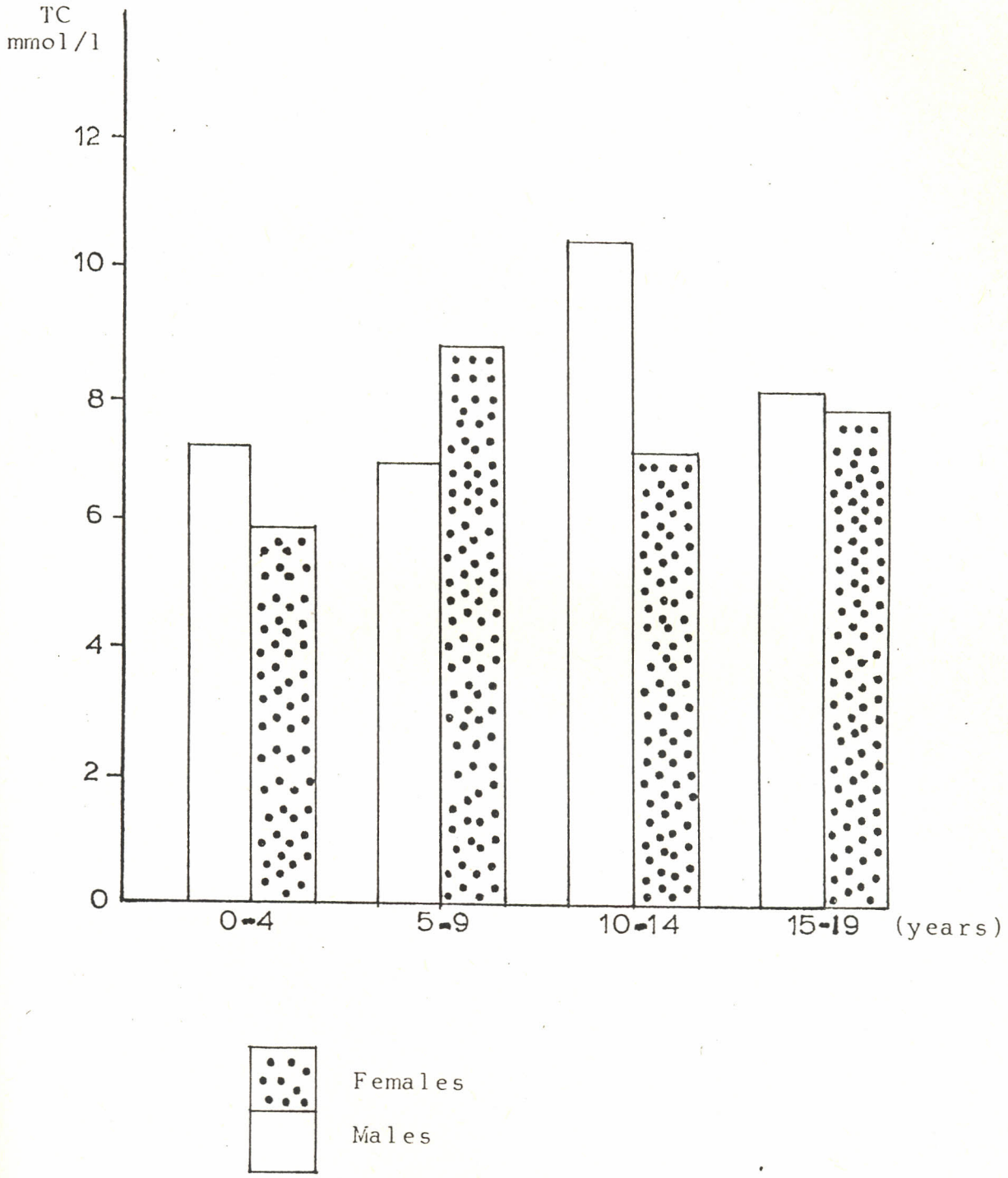


Figure 3: Patient's mean serum TC by age group and sex

Table 10: Mean serum lipids of steroids treated and non-steroid treated patients.

Lipid / Patients	TC	TG	LDL	VLDL	HDL
Steroid treated	7.1±2.4	2.0±0.8	4.8±1.9	1.0±0.1	0.8±0.1
Non-steroid treatment	7.7±3.5	4.3±3.5	4.7±3.5	1.2±0.6	0.8±0.2
P-value	<0.1	<0.001	<0.05	<0.001	-
	NS	S	S	S	NS

Figure 4 compares the variation in lipid fractions between the corticosteroid treated patients, controls and the patients who were not treated with corticosteroids. TC was highest in the non-steroid treated patients as was the TG. There was little difference in the LDL, VLDL and HDL between the treated and untreated patients. HDL was highest in the controls.

Table 11 illustrates the distribution of mean serum lipid fractions in different histopathological lesions. Patients with the diffuse proliferative lesions had the highest lipid levels followed by those with crescenteric, end stage renal disease and mesangioproliferative in order of decreasing levels. The lipid fraction alterations correlated with the severity of glomerular lesions. HDL was not affected by the type of glomerular lesion.

Correlations between lipid profiles and other biochemical parameters.

a) Creatinine.

Figure 5 illustrates the inverse relationship between the HDL and log creatinine, $r=0.09$ and $p<0.01$.

Figure 6 illustrates the relationship between TG and log creatinine. No significant correlations is observed $r=0.02$ and $p>0.05$. Similarly no correlations were observed between creatinine and TC or VLDL.

b) BUN

Figure 7 depicts the relationship between log TC and log BUN.

There is an apparent positive correlation, $r=0.02$ and $p<0.01$.

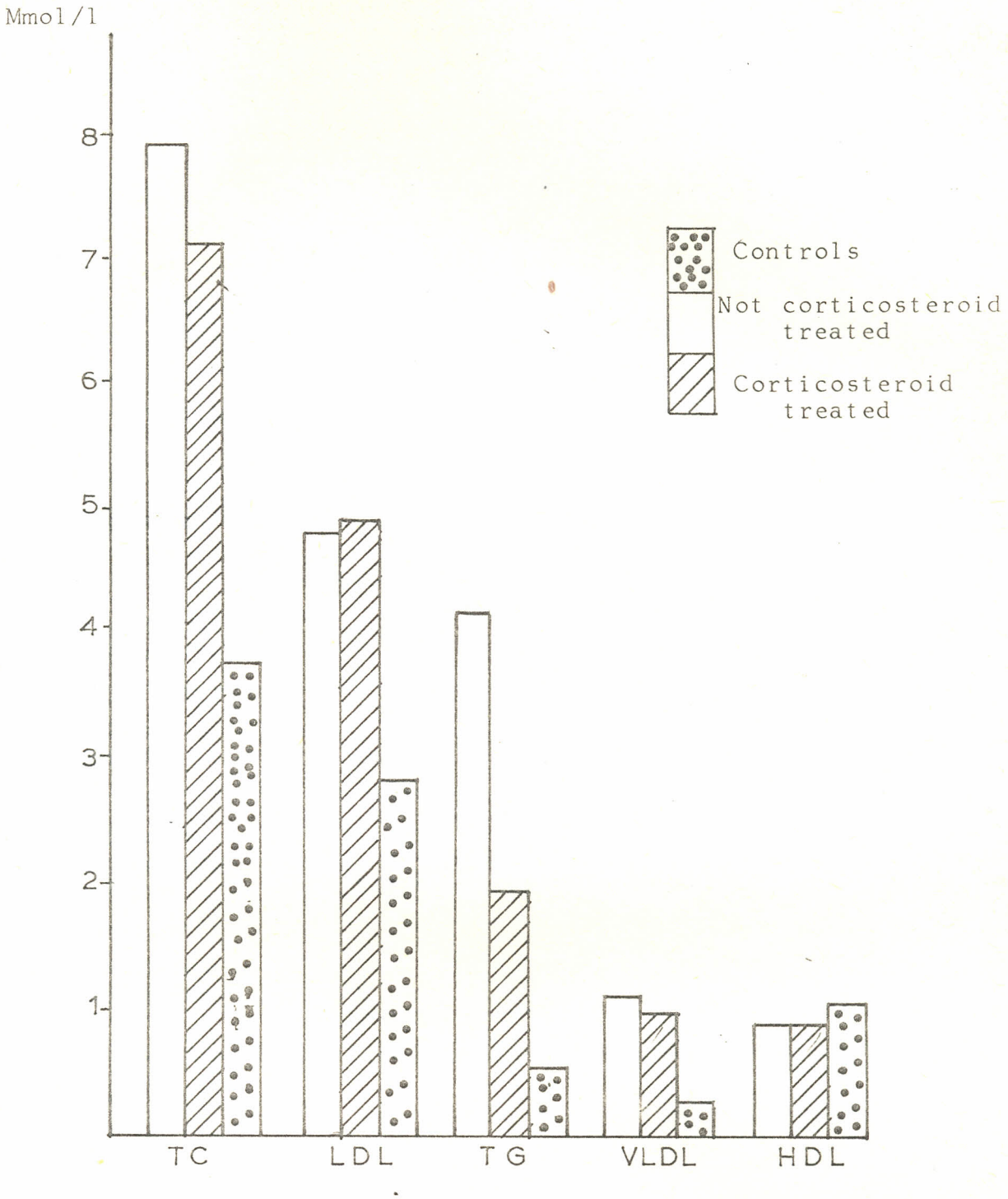


Figure 4: Distribution of mean serum lipids of the controls, steroid treated and non-steroid treated patients.

Table 11: Lipid vs Histopathological Lesions.

Lipid / Histological lesion	TC	TG	LDL	VLDL	HDL
Diffuse proliferative glomerulo-nephritis	9.5±2.2	3.0±0.7	7.8±1.8	1.2±0.4	0.8±0.4
Crescenteric glomerulo-nephritis	8.9±5.4	2.6±1.2	6.9±5,1	1.4±0.4	0.7±0.1
End stage renal Disease	8.8±4.6	2.4±0.9	5.6±4.7	1.3±0.7	0.8±0.2
Mesangiocapillary glomerulonephritis	8.5±4.6	2.4±0.9	5.6±4.7	1.3±0.7	0.8±0.2
Focal glomerulo-sclerosi (FGS)	8.3±2.9	2.3±1.1	6.2±2.7	0.9±0.6	0.75±0.15
Membranoprolife-rative glomerulo-nephritis	7.1±1.4	2.3±0.3	4.6±0.7	1.0±0.1	0.7±0.1
Mesangioprofera-tive glomerulo-nephritis	5.9±0.4	1.7±0.4	3.8±1.0	1.3±0.8	0.7±0.1

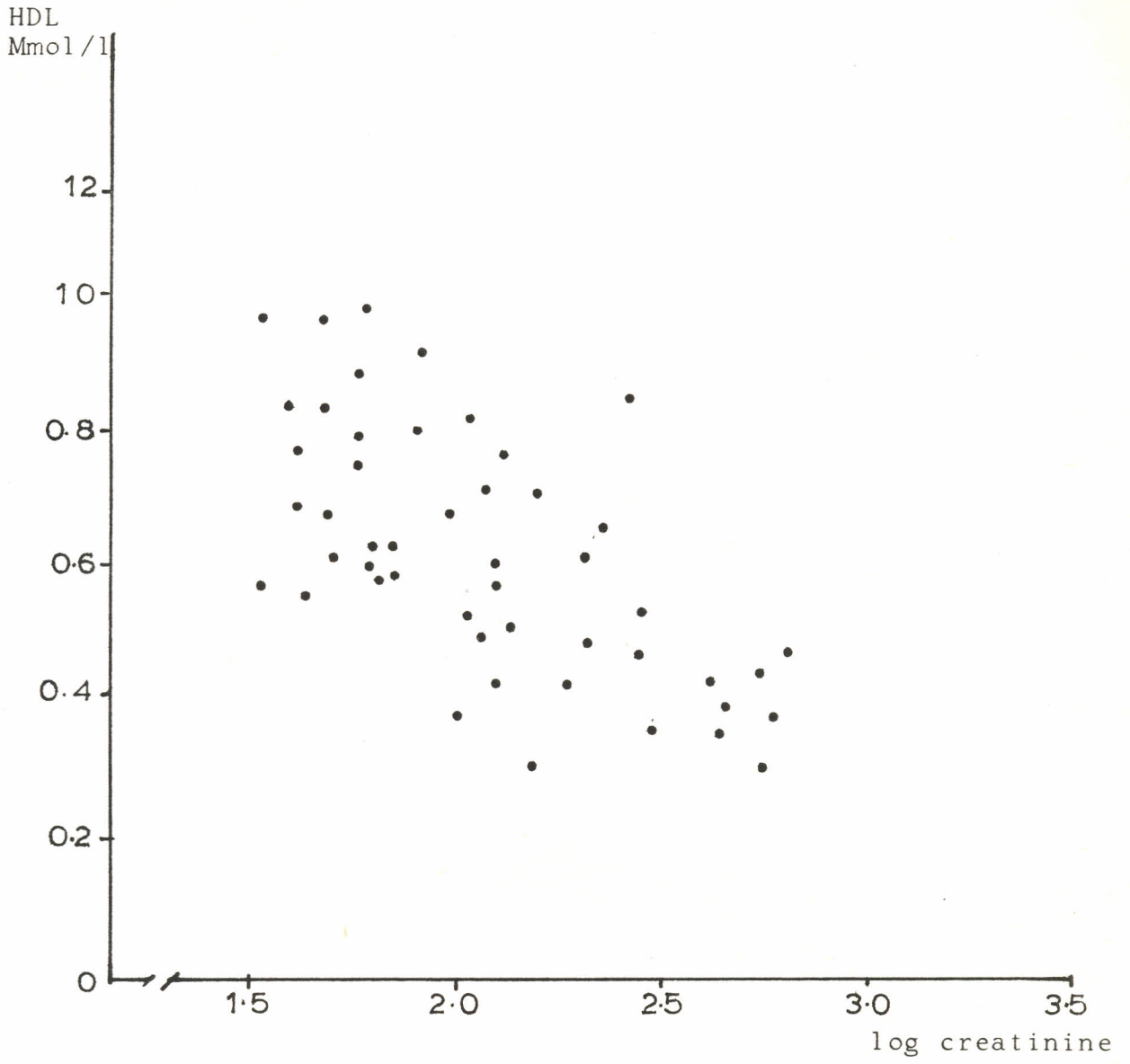


Figure 5: HDL versus log creatinine.

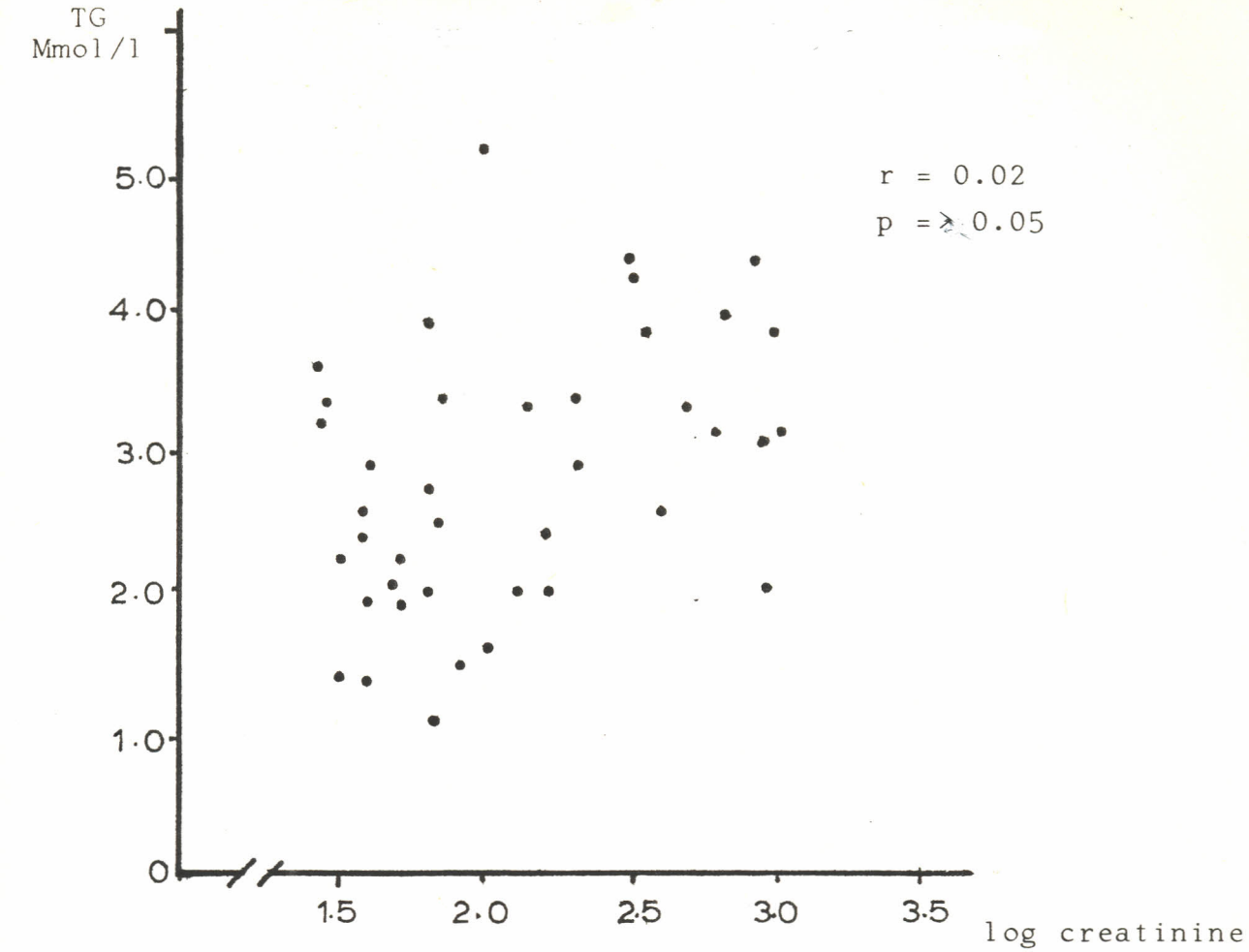


Figure 6: TG versus long creatinine

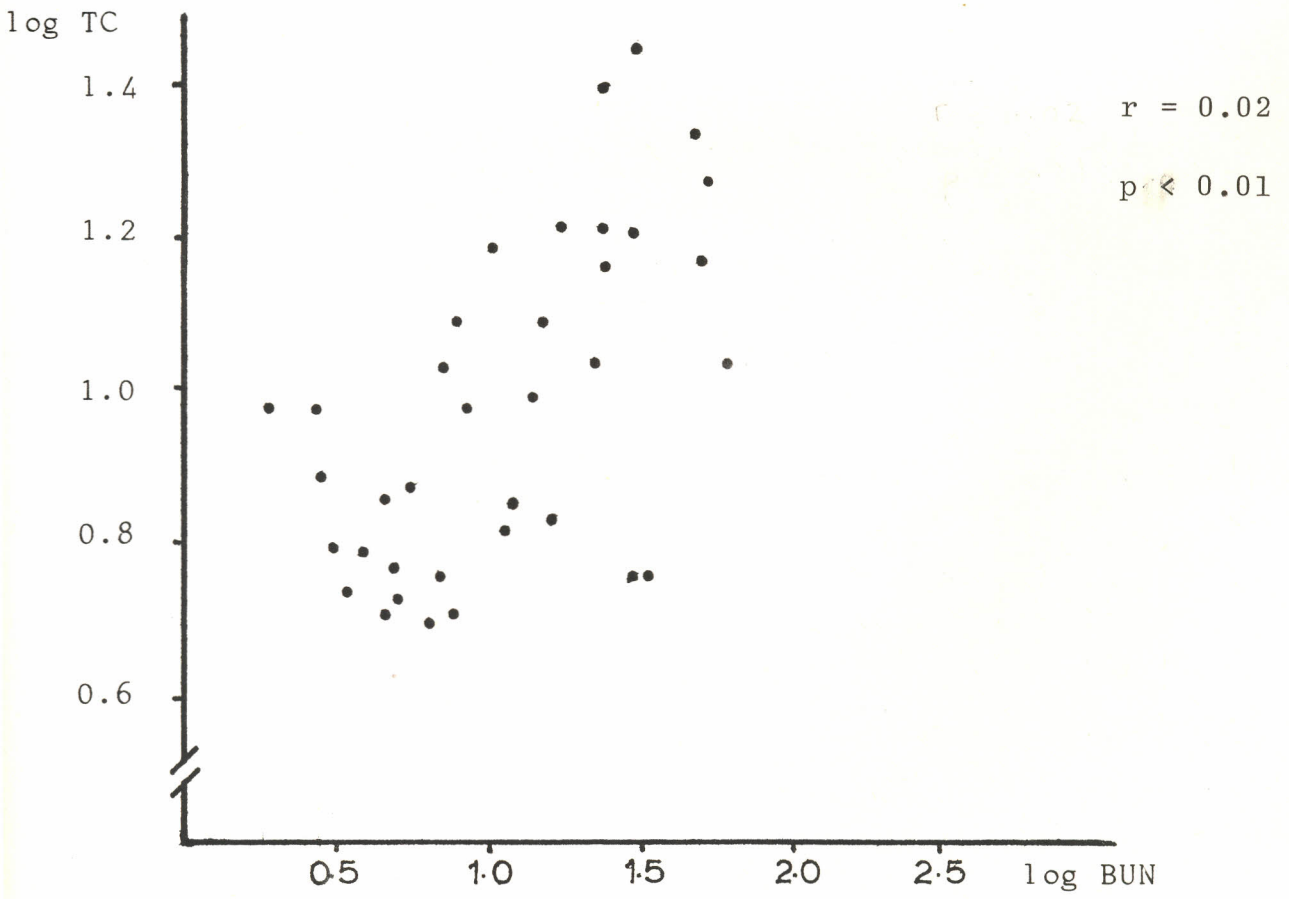


Figure 7: log TC versus log BUN

Figure 8 illustrates the relationship of TG and log BUN. It shows a direct relationship between TG and log BUN. $r=0.65$ and $p<0.001$.

No significant correlations were noted between BUN and HDL or VLDL.

c) Albumin.

Figure 9-11 illustrate the relationships between serum albumin and the lipid fractions.

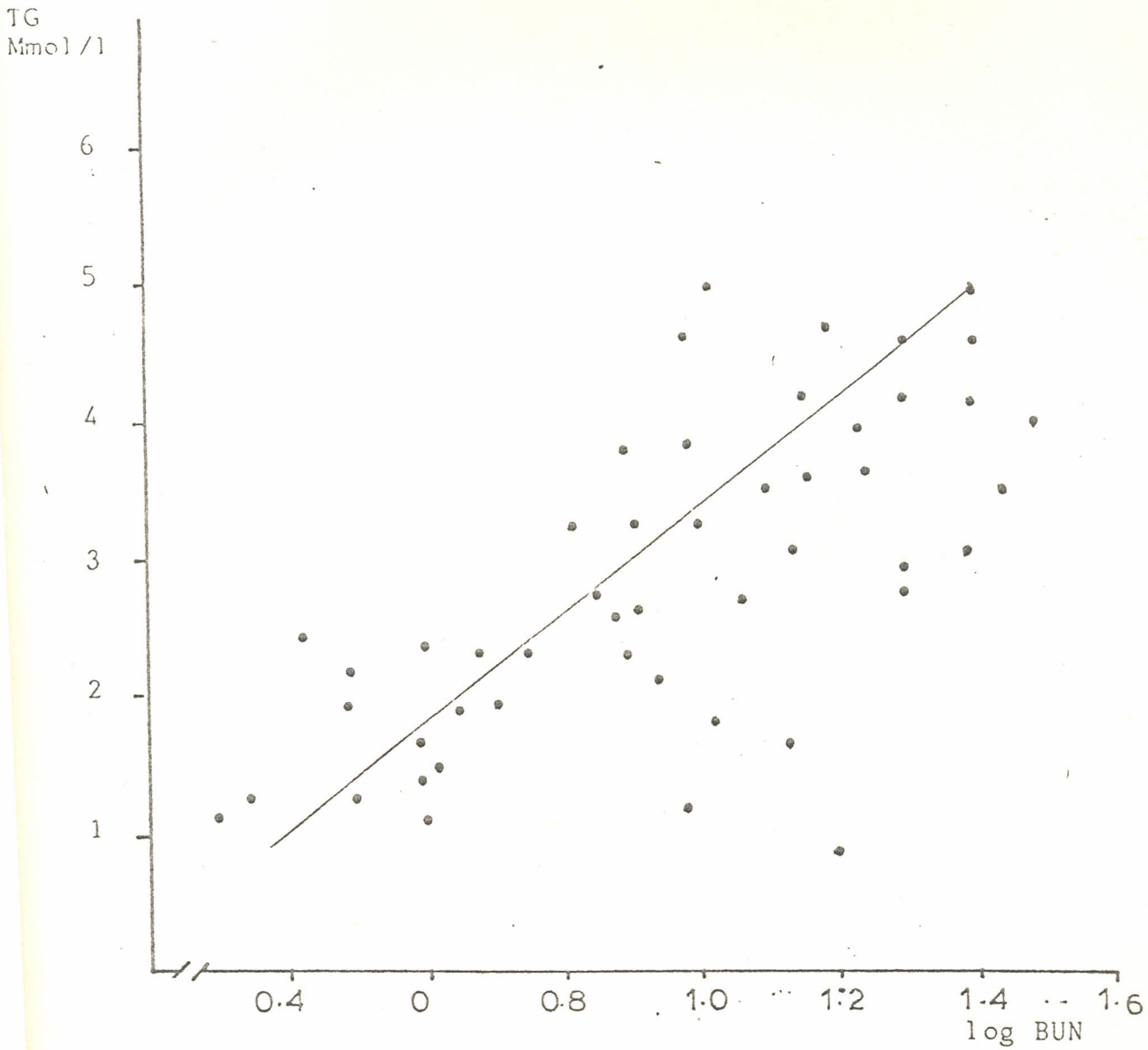
Figure 9 illustrates the correlation between VLDL and albumin it shows a negative correlation between the two $r=-0.67$ and $p<0.01$

Figure 10 shows the relationship between log VLDL and albumin. There is a negative correlation $r=-0.9$ and $p<0.01$.

Figure 12 illustrates the relationship between HDL and albumin, a direct correlation is evident $r=0.72$ and $p<0.01$.

d) Protein.

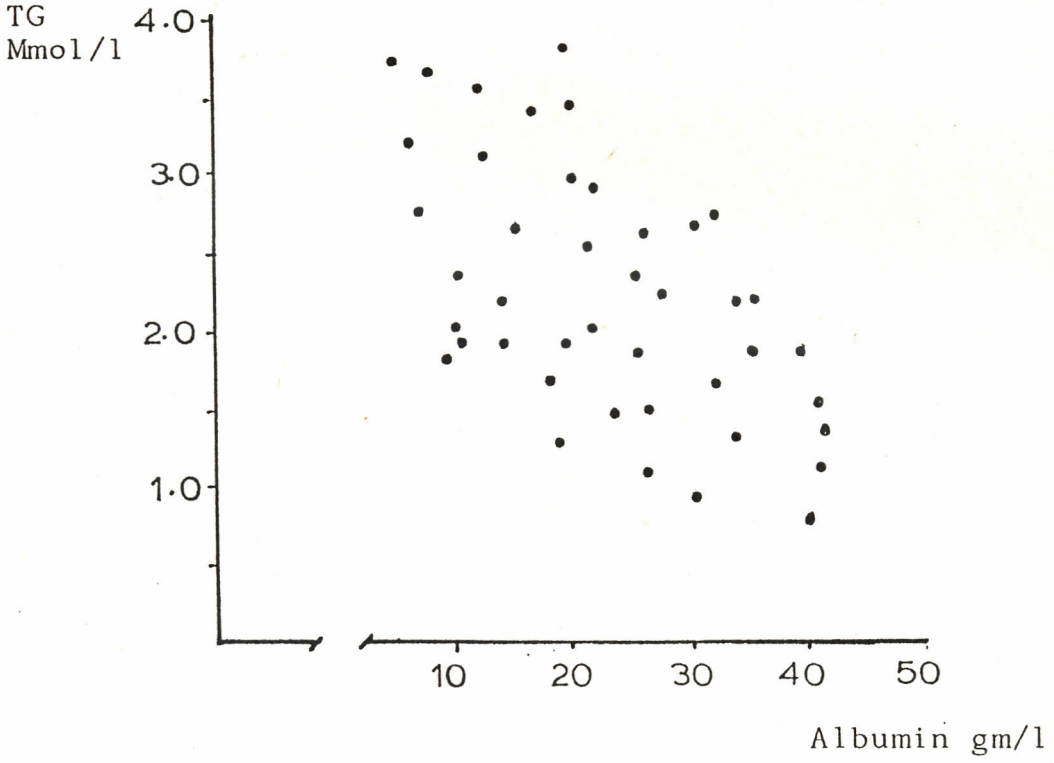
No meaningful relationships could be established between the lipid fraction alterations and the total serum protein.



r = 0.65

p = 0.001

Figure 8: TG versus log BUN



r = -0.67

p < 0.001

Figure 9: TG versus Albumin

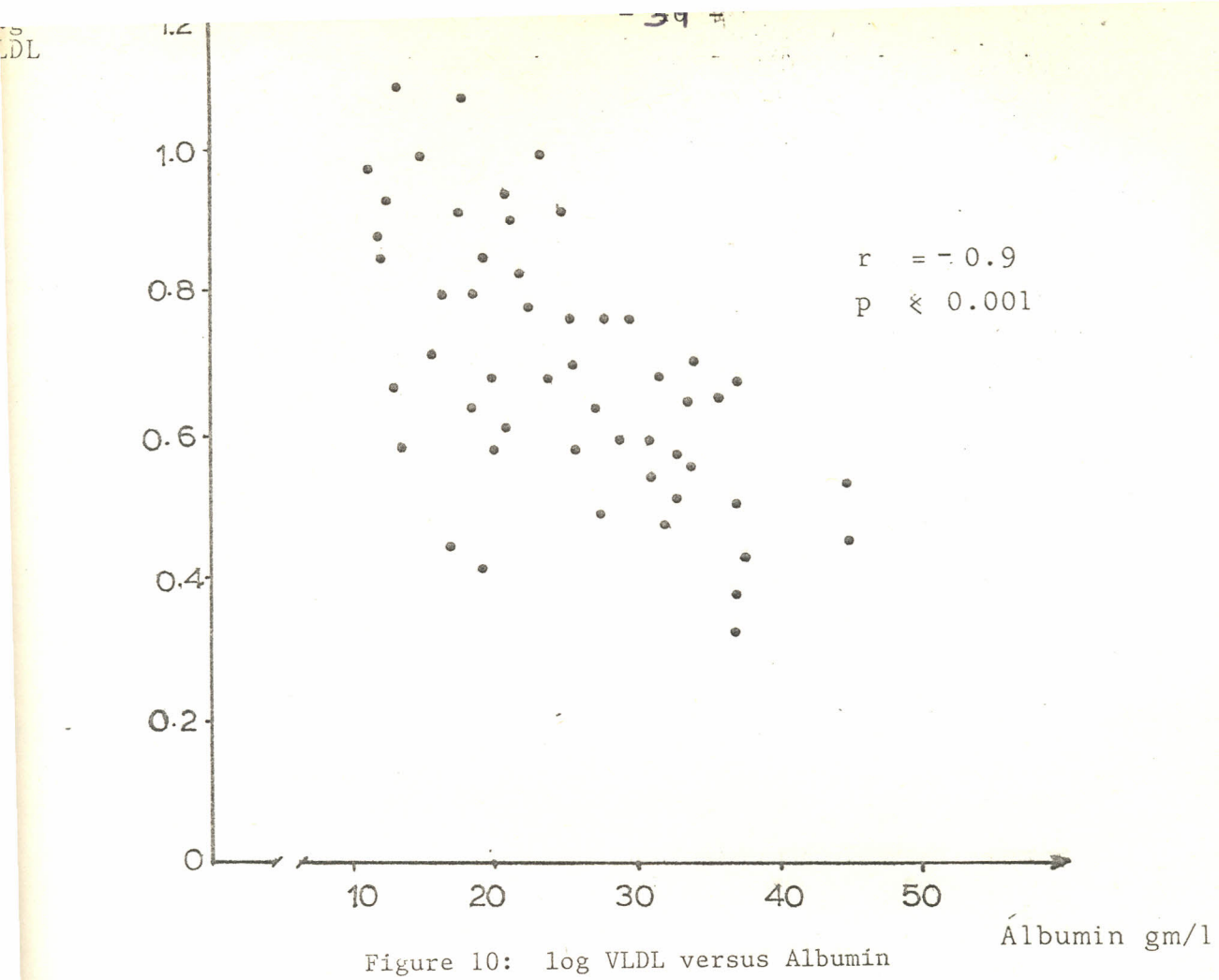


Figure 10: log VLDL versus Albumin

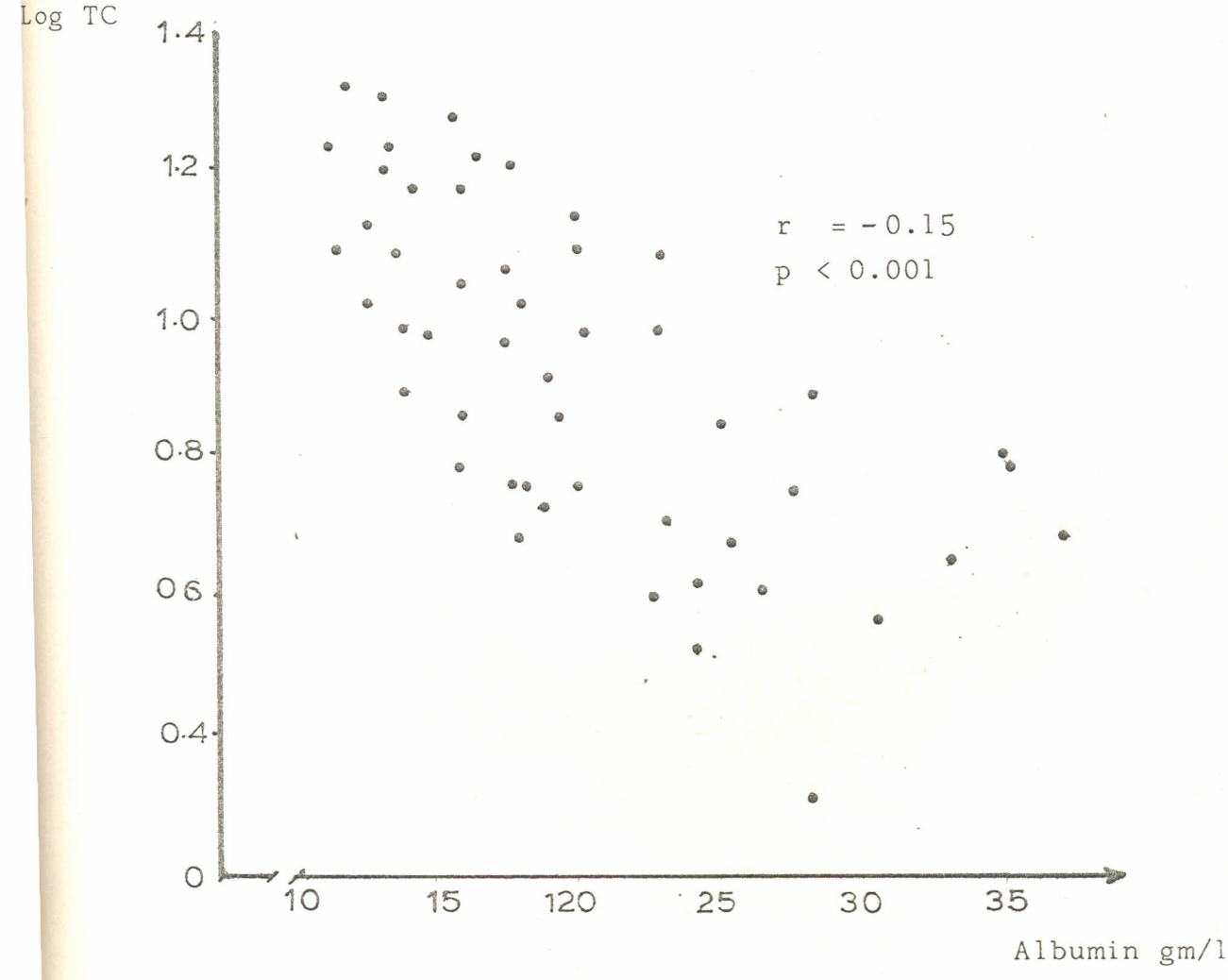


Figure 11: Log TC versus Albumin

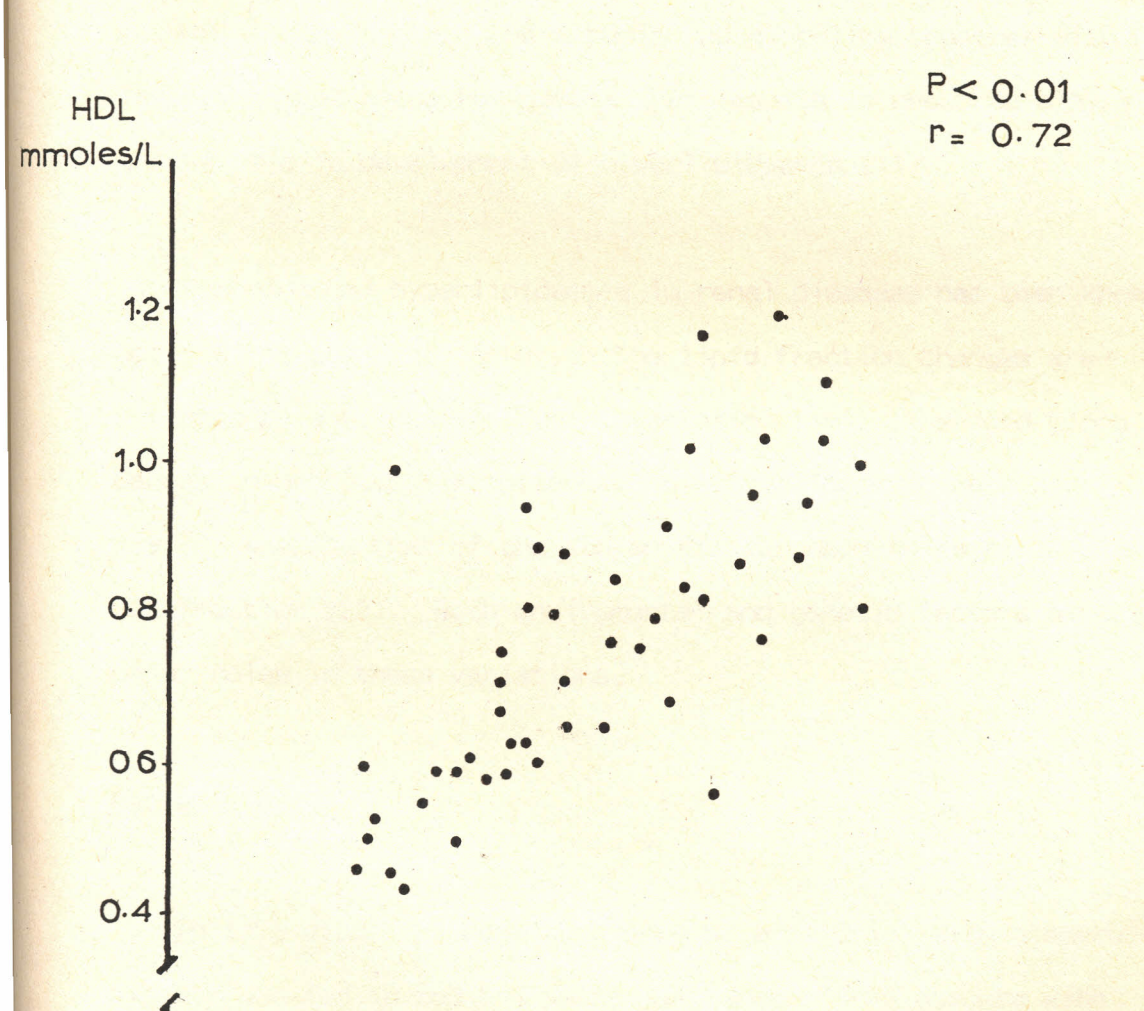


Figure 12 HDL Versus Albumin

D I S C U S S I O N.

The primary pathological process that occurs in glomerular disease is a change in the permselectivity of the glomerular basement membrane allowing passage into the urine of macromolecules that are normally excluded from the glomerular ultrafiltrate (60). The main molecules affected are the albumin and globulins together with HDL. The consequent hypoalbuminaemia that results is known to play a causal role in development of hyperlipidaemia (11).

Pathological hyperlipidaemia in renal diseases has been known to occur since the last century. The lipid fraction changes are affected by age, sex and racial variation (38). The cord blood of Caucasion neonates for instance, have been found to be richer in HDL (39,40) whereas that of the Kenyan African neonate is richer in the LDL fraction (22). Both enviromental and genetic factors also play major roles in these variations.

Patients data.

In this study the peak age range of affliction with glomerular disease occured in the 5-9 years age range. This concurs with similar findings from West Africa (42,43) but differs from the American and European studies in which the peak age has been found to be 2 and 3 years of age respectively (43). The male to female ratio in our patients was 2:1 which also agrees with other studies (41-43). Fifty two percent of the study patients had pure nephrosis while 48% had a nephritic nephrosis. The majority of the patients

(92%) had moderate or severe proteinuria. Both oedema and proteinuria were common physical findings occuring in 78% and 92% of patients respectively. Hypertension and haematuria occurred in 36%.

and 34% of the study patients. Splenomegaly and hepatomegaly were observed in 18% and 16% respectively. The patients who exhibited these two later features hailed from malarious areas.

Alteration in lipid and lipoprotein fractions was observed in 36/50 (72%) of patients. The patients with severe proteinuria also had the highest alterations in the lipid fractions.

Histopathological lesions.

The histopathological changes that occur in glomerular disease depend on the nature and severity of renal insult as well as the causative agent. Work done in Western countries has shown the minimal change glomerulonephritis (MCGN) to be the most common histopathological lesion in childhood glomerular disease (24). In Africa earlier work puts the same lesion at about 25-30% of all glomerular lesions in both children and adults (21,41). Malaria nephropathy is a lesion commonly seen in West Africa (20,42-46).

In this study the commonest histopathological lesion seen was the focal glomerulosclerosis which comprised 22.7% of the biopsies, followed by mesangiocapillary glomerulonephritis, mesangioproliferative glomerulonephritis and crescenteric glomerulonephritis which is usually associated with rapidly progressive glomerulonephritis. Malaria nephropathy was noted in one

patient this could be explained by the geographical location of the study area being outside the malarious endemic area. Similarly tuberculous nephropathy was observed in one patient. These two later observations highlight the importance of tropical diseases in the causation of glomerular disease.

The more severe glomerular lesions such as diffuse proliferative, mesangiocapillary and crescenteric glomerulonephritides showed marked alterations in the levels of lipid fractions. All lipid fraction levels apart from that of HDL were elevated far beyond the normal levels. On the other hand HDL levels were lowered, this being due to the increased urinary loss of HDL.

None of the renal biopsies exhibited the minimal change glomerulonephritis lesion. This might probably be due to the improved medical care at the peripheral health units so that the patients with this type of lesion are managed well there and do not have to be referred to Kenyatta National Hospital.

The extent of glomerular insult is responsible for the severity of disease and the associated hyperlipoproteinaemia is related to the hypoalbuminaemia and albuminuria that ensues especially in the nephrotic syndrome. Ridon et al (25) found significant correlations between the renal histopathology and both plasma creatinine and creatinine clearance. They concluded that renal tubular damage other than structural glomerular damage determined the degree of renal function impairment. On the other hand Katafuchi et al (48) in Japan found significant positive correlation between serum creatinine and glomerular index (a measure of the extent of glomerular damage).

Both Hutt (49) and Parrish(50) showed that the glomerular lesions correlated well with renal function. This study shows that the more severe glomerular lesions also exhibited both the highest alterations in lipid and lipoprotein fractions as well as the most marked derangement of both BUN and creatinine, these alterations being most prominent in patients who had diffuse proliferative, end stage and crescenteric glomerulonephritis. (Table 10). The creatinine levels in these patients with these lesions were above 300umoles/l.

Biochemical parameters and lipid profiles.

As indicated above in the results, 72% of all study patients had altered biochemical parameters when compared to the normal controls. The inherent hyponatraemia is consequent to the fluid retention. The significant elevation in both BUN and creatinine is secondary to the associated renal failure which is variable in the patients. Hypoalbuminaemia is due to the massive proteinuria that accompanies the glomerular damage especially in the nephrotic syndrome. Likewise the hypoproteinaemia can be explained on the same grounds.

The patients with markedly elevated BUN and creatinine also exhibited highest elevations in lipid and lipoprotein fractions. It is only HDL which shows a negative correlation to creatinine as there were no significant correlations noted with other lipoproteins or lipids.

BUN on the other hand exhibits positive correlations with both TC, TG and HDL. Thus elevations either in BUN or creatinine would be possible indicators of altered lipid fractions.

Earlier work by Abdallah et al (1) at K.N.H. on adult African Kenyan patients with CRF, showed them to have elevated cholesterol and triglycerides. The levels being 4.99 mmol/l and 4.72 mmol/l respectively (converted from mg%). The levels in the normal controls were 4.72 $\pm$ 0.5 mmol/l and 0.32 + 0.08 mmol/l. Ojwang et al (22) working on normal healthy adults at the same place found the lipid profiles to be about the same levels. He also determined normal lipoprotein levels for both male and female, normal healthy adult subject. There were no significant differences between the two groups except for the LDL fraction which was significantly higher in the males. This study shows that the lipid fractions are significantly lower in the children when compared with adult levels. These being TC 3.7 $\pm$ 0.8 mmol/l, TG 0.64 $\pm$ 0.2 mmol/l, LDL 2.4 $\pm$ 0.64 mmol/l and VLDL 0.32 $\pm$ 0.1 mmol/l.

Cohen et al (8) found patients with the nephrotic syndrome to have decreased HDL and albumin levels whereas the triglycerides were elevated. Our study exhibits similar observations. The HDL have been noted to be disproportionately low with respect to the other lipoproteins in most active glomerulopathies (52,53). This may be due to increased urinary loss of HDL. The HDL level is said to be inversely proportional to the risk of developing coronary vascular diseases (53,54). It has been suggested that the levels of the apolipoproteins are strongly related to clinical disease (55,56). In this study it was not possible to measure the apolipoproteins.

Table 7 which compares the lipid fractions between normal male and female subjects in different environments, it brings out the effects the of both age and environment on the lipid profiles. The subjects in the Western world had the highest lipid levels when compared to subjects in a tropical environment. The children in the tropical environment had significantly lower levels when compared to the adults in the same environment.

The observed differences between subjects in the tropical setting and those in the Western world are probably contributed to by dietary factors.

The patients treated with corticosteroids had significantly lower TG and VLDL fraction elevations than the patients who were not on corticosteroid therapy. The effect of corticosteroids on TG and VLDL is probably indirect being mediated through enhanced activation of cellular lipase by lipid-mobolising hormones such as catecholamines and pituitary peptides. As noted in the results, the HDL fraction was not effected by corticosteroid therapy. The reason for this is not clear.

Since many studies correlate high cholesterol levels with atherosclerotic cardiovascular disease, serum lipid and lipoprotein levels in patients with glomerular disease deserve serious consideration (57,58). Dietary therapy has been shown to be beneficial in treating hyperlipidaemia in non-transplant populations (59,60). Polyunsaturated dietary fat have been successfully used to treat hyperlipidaemia. Dietary fish oil eicosapentenoic Acid (EPA) has been shown to reduce hyperlipidaemia in CRF (58) as well as slowing the progression of the disease. Chemotherapy has also been used in treating hyperlipidaemia but the drugs used such as clofibrate (atromid-s) are not without side effects.

C O N C L U S I O N.

This study has demonstrated that:-

1. Most of the children with glomerular disease are aged 5-9 years, the males being afflicted twice as frequently as the females.

2. In the clinicopathological classification it was noted that both haematuria and hypertension are frequent features in these patients making up 34% and 36% respectively.

3 Most of these patients have pure nephrosis 26 (52%) this being slightly more frequent than nephritic nephrosis 24 (48%).

4. Of all the patients on whom a histopathological diagnosis was made, 10 (22.7%) had focal glomerulosclerosis this being the predominant glomerular lesion.

5. Children with glomerular diseases particularly the nephrotic syndrome have significantly elevated serum lipid and lipoprotein fractions. In this study, 36(72%) patients had altered lipid and lipoprotein fractions.

6. The HDL fraction is significantly lowered in all patients.

7. An inverse correlation is observed between serum lipids and albumin except for HDL which has a direct correlation.

8. A direct correlation exists between TC and TG with both the creatinine and BUN.

9. There is an apparent direct relationship between the severity of glomerular lesion and the degree of lipid and lipoprotein alterations.

RECOMMENDATIONS.

1. There is need for more work to be done in patients particularly children with glomerular diseases so as to establish the aetiological factors causing the renal insult. This will lead to prevention of the development of glomerular disease in the instances where a treatable causative agent is found.

2. The importance of secondary hypoalbuminaemia as seen in the severe forms of nephrosis should not be underated. Prompt treatment with fresh frozen plasma or salt free human albumin is strongly advocated for as a life saver.

4. All patients with glomerular disease should have their serum lipid profiles monitered.

5. That the renal team together with the hospital dieticians design and formulate a dietary protocol to be used in patients exhibiting hyperlipidaemia. All the patients with established hyperlipidaemia be started on the formulated dietary measures.

6. The lipid profiles be monitered regularly in these patients so as to decide on a possibility of chemotherapy and/or dietary therapy when the need arises.

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APPENDIX I

Name IP.No.

Tribe

Age (yrs)

Sex:Male/Female

Dry Weight (Kgs)

Height (cms)

	Absent	Mild	Moderate	Severe	Dubious
Oedema					
Ascites					
Splenomegaly					
Hepatomegaly					
Proteinuria					
Haematuria					

Bp	Initial	Mistudy	Late

Duration of illness (months)

Type of medications(s) being taken

Clinical diagnosis

Past Medical Histoty

Underlying disease.

APPENDIX II.

Laboratory results/biodata

Histological diagnosis:

Clinical diagnosis

1. Blood

BUN..... mmol/L

Na^+..... mmol/L

K^+..... mmol/L

Cl ..... mmol/L

Creatinine ..... mmol/L

Protein ..... gm/L

Albumin..... gm/L

Total cholesteroal .. mmol/L

Triglycerides ..... mmol/L

HDL ..... mmol/L

LDL ..... mmol/L

VLDL ..... mmol/L

2. Urine:

Proteinuria .....

Sugar .....

RBC.....

RBC cast .....

Bacteria .....

APPENDIX III.

Classification criteria for pure nephrosis and nephritic nephrosis (ISKDC).

1) Nephrotic Nephrotics:-

These were patients who had in addition to the nephrotic syndrome either:

i) Two or more of the following features.

a) Persistent haematuria (microscopic of macroscopic)

b) Significant azotaemia (BUN > 100 mg/dl) on at least one occassion or a BUN which was repeatedly measured above the upper limit of normal (> 40mg/dl).

c) Sustained hypertension.

ii)Renal histological evidence of proliferative glomerulo nephritis.

2) Pure nephrotics

These were patients who had the following features:

i) Haematuria was either mild, transient or absent.

ii) Azotaemia was absent or mild (50mg/dl) or transient.

iii) Sustained hypertension was not documented