RESULTS

Results of the clinical study :

The results of the clinical examination of our patients were as follows :

Group I : Included 15 patients suffering from rheumatoid arthritis, all of them had poly-articular involvement, with bilateral knee effusion. They were 10 females (66.7%) and 5 males (33.3%), their ages ranged between 32 and 60 years, with a mean of 43.4 ± 3.55 years.

The disease duration ranged between 1 and 5 years, with a mean of 3.2 ± 0.58 years.

The duration of morning stiffness ranged between 15 and 80 minutes, with a mean of 36.33 ± 8.1 minutes.

The functional capacity according to **Steinbroker et al. (1949)** classification, was grade I in 6 patients, grade II in 7 patients and grade III in 2 patients.

On calculating the articular index for the patient according to the modified articular index **(Ritchie et al., 1968)**, it ranged between 5 and 45 with a mean of 22.46 ± 4.88.

The grip strength of the patient's right hand ranged between 60 and 130 mmHg., with a mean value of 98.6 ± 9.37 mmHg. while the grip strength of the left hand ranged between 70 and 150 mmHg., with a mean of 96.6 ± 11.7 mmHg **Table (1).**

Group II : Included 15 patients suffering from osteoarthritis of the knee, all of them had synovial effusion. They were 8 females (53.3%) and 7 males (46.7%), their ages ranged between 41 and 61 years, with a mean of 52.06 ± 2.79 years.

The disease duration ranged between 1 and 11 years, with a mean of 5.4 ± 1.45 years. **Table (2).**

Results of the laboratory study :

A- Rheumatoid arthritis group :

The erythrocyte sedimentation rate (E.S.R) of all the patients ranged between 21 and 130 mm in the first hour, with a mean value of 68.8 ± 14.2 mm/hour.

The haemoglobin concentration ranged between 8 and 10 gm/dl, with a mean value of 9.16 ± 0.27 gm/dl.

The latex fixation test for rheumatoid factor was positive in 10 patients (66.7%) and negative in 5 patients (33.3%).

The red blood cells count : it ranged between 2.400.000 and 4.450.000/mm^3,with a mean value of 3.483.333 ± 0.288.636/mm^3.

The white blood cells count : it ranged between 4.000 and 8.500/mm^3, with a mean value of 6.560 ± 0.593/mm^3. **Table (3).**

The plasma fibronectin level ranged between 17 and 35 mg/dl, with a mean value of 26.53 ± 2.75 mg/dl.

The synovial fluid fibronectin level ranged between 27 and 50 mg/dl, with a mean value of 39.93 ± 3.17 mg/dl. **Table (4).**

B- Osteoarthritis group :

The erythrocyte sedimentation rate (E.S.R) of all the patients ranged between 10 and 29 mm. in the first hour, with a mean value of 21.66 ± 2.85 mm/hour.

The haemoglobin concentration ranged between 11.8 and 13.6 gm/dl, with a mean value of 12.63 ± 0.25 gm/dl.

The red blood cells count:it ranged between 2.700.000 and 4.460.000/mm^3, with a mean value of 3.949.333 ± 0.216. 152/mm^3.

Table (2).

The plasma fibronectin level ranged between 17 and 35 mg/dl, with a mean value of 25.4 ± 2.39 mg/dl.

The synovial fluid fibronectin level ranged between 22 and 45 mg/dl, with a mean value of 30.73 ± 3.08 mg/dl. **Table (5).**

Table (1): Results of the clinical data of patients with rheumatoid arthritis.

Case number	Age (years)	Sex	Disease duration (years)	M.S. (minutes)	F.C.	A.I	Grip strength (mmHg)	
							Right hand.	Left hand.
1	44	F	3	30	II	25	100	90
2	41	F	5	70	III	45	90	80
3	40	F	2	20	I	14	120	140
4	45	F	4	45	II	30	80	90
5	40	F	5	30	III	22	90	70
6	37	F	5	30	II	19	130	70
7	46	F	4	30	I	20	80	100
8	52	F	3	50	II	30	90	80
9	39	F	1	15	I	5	110	130
10	50	F	3	30	I	14	100	120
11	32	M	3	30	I	25	120	100
12	55	M	2	30	II	24	110	70
13	38	M	3	80	II	40	70	90
14	32	M	4	40	II	19	60	70
15	60	M	1	15	I	5	130	150
$\bar{X}$ SD SE	43.4 ± 7.81 ± 3.55		3.2 ± 1.27 ± 0.58	36.33 ± 17.83 ± 8.1		22.46 ± 10.73 ± 4.88	98.67 ± 20.61 ± 9.37	96.67 ± 25.73 ± 11.7

M.S. = Morning stiffness
F.C. = Functional capacity
A.I. = Articular index

$\bar{X}$ = Mean
S.D. = Standard deviation
S.E. = Standard error

M = Male
F = Female

Table (3): Results of laboratory data of patients with rheumatoid arthritis.

Case number	E.S.R. (mm/ hour) in the first hour	H.B. gm/dl	R.F.	RBCs/mm^3	WBCs/mm^3
1	80	8.0	+ve	3.820.000	7.500
2	120	8.9	+ve	2.900.000	8.200
3	60	9.5	-ve	2.800.000	6.000
4	65	9.9	+ve	2.800.000	5.500
5	85	9.0	+ve	3.900.000	7.800
6	65	9.0	+ve	3.250.000	7.000
7	51	10.0	-ve	4.400.000	5.500
8	95	9.5	+ve	3.400.000	8.500
9	25	9.5	-ve	4.450.000	5.500
10	25	10.0	-ve	4.330.000	5.300
11	50	8.5	+ve	3.600.000	5.800
12	85	8.6	+ve	2.400.000	7.000
13	130	8.7	+ve	2.800.000	8.500
14	75	8.5	+ve	4.000.000	6.300
15	21	9.8	-ve	3.400.000	4.000
$\bar{X}$	68.8	9.16		3.483.333	6.560
SD	± 31.24	± 0.61		± 0.634.672	± 1.304
SE	± 14.2	± 0.27		± 0.288.634	± 0.593

E.S.R.= Erythrocyte sedimentation rate

H.B. = Haemoglobin

R.F. = Rheumatoid factor

RBCs = Red blood corpuscles

WBCs = White blood corpuscles

$\bar{X}$ = Mean

S.D. = Standard deviation

S.E = Standard error

Table (4): Plasma and synovial fluid fibronectin concentrations in patients with rheumatoid arthritis.

Case Number	Plasma (Fn.) mg/dl	Synovial fluid (Fn.) mg/dl
1	30	45
2	28	32
3	24	44
4	25	50
5	22	27
6	20	48
7	34	43
8	31	28
9	22	37
10	35	38
11	19	40
12	35	46
13	22	36
14	17	48
15	34	37
$\bar{X}$	26.53	39.93
SD	$\pm$ 6.05	$\pm$ 6.97
SE	$\pm$ 2.75	$\pm$ 3.17

FN. = Fibronectin

$\bar{X}$ = Mean

SD = Standard deviation

SE = Standard error

Table (5): Plasma and synovial fluid fibronectin concentrations in patients with osteoarthritis.

Case Number	Plasma (Fn.) mg/dl	Synovial fluid (Fn.) mg/dl
1	25	45
2	21	26
3	26	33
4	24	25
5	30	41
6	35	31
7	27	36
8	25	23
9	17	29
10	18	24
11	35	22
12	26	32
13	27	34
14	18	23
15	27	37
$\bar{X}$	25.4	30.73
SD	$\pm$ 5.26	$\pm$ 6.79
SE	$\pm$ 2.39	$\pm$ 3.08

FN. = Fibronectin

$\bar{X}$ = Mean

SD = Standard deviation

SE = Standard error

Statistical evaluation revealed insignificant correlation between the synovial fluid or plasma fibronectin concentrations in R.A. patients and any of the clinical or laboratory parameters ($P > 0.05$).
Table (6).

Statistical evaluation revealed a highly significant positive correlation between the plasma fibronectin concentrations in R.A. patients with their ages ($P < 0.001$).
Table (6).

Statistical evaluation revealed insignificant correlation between the synovial fluid or plasma fibronectin concentrations in O.A. patients and any of the clinical or laboratory parameters ($P > 0.05$).
Table (7).

Table (6): Correlation coefficients between synovial and plasma (FN.) levels in R.A patients with the clinical and laboratory data of the patients.

		Plasma (Fn.) mg/dl	Synovial fluid (Fn.) mg/dl
Age (years)		0.9 **	- 0.15 *
Disease duration (years)		-0.29 *	- 0.01 *
M.S. (minutes)		-0.13 *	- 0.25 *
F.C.		0.17 *	0.26 *
A.I		-0.04 *	- 0.18 *
Grip strength (mmHg)	Right hand	0.14 *	0.06 *
	Left hand	0.25 *	- 0.03 *
E.S.R. (mm/hour)		-0.17 *	- 0.24 *
HB gm/dl		0.4 *	- 0.1 *
R.F.		0.32 *	0.09 *
RBCs/mm^3		0.005 *	- 0.16 *
WBCs/mm^3		- 0.17 *	- 0.39 *

* = P >0.05 insignificant correlation

** = P <0.001 highly significant correlation

Table (7): Correlation coefficients between synovial and plasma (FN.) levels in O.A. patients with the clinical and laboratory data of the patients.

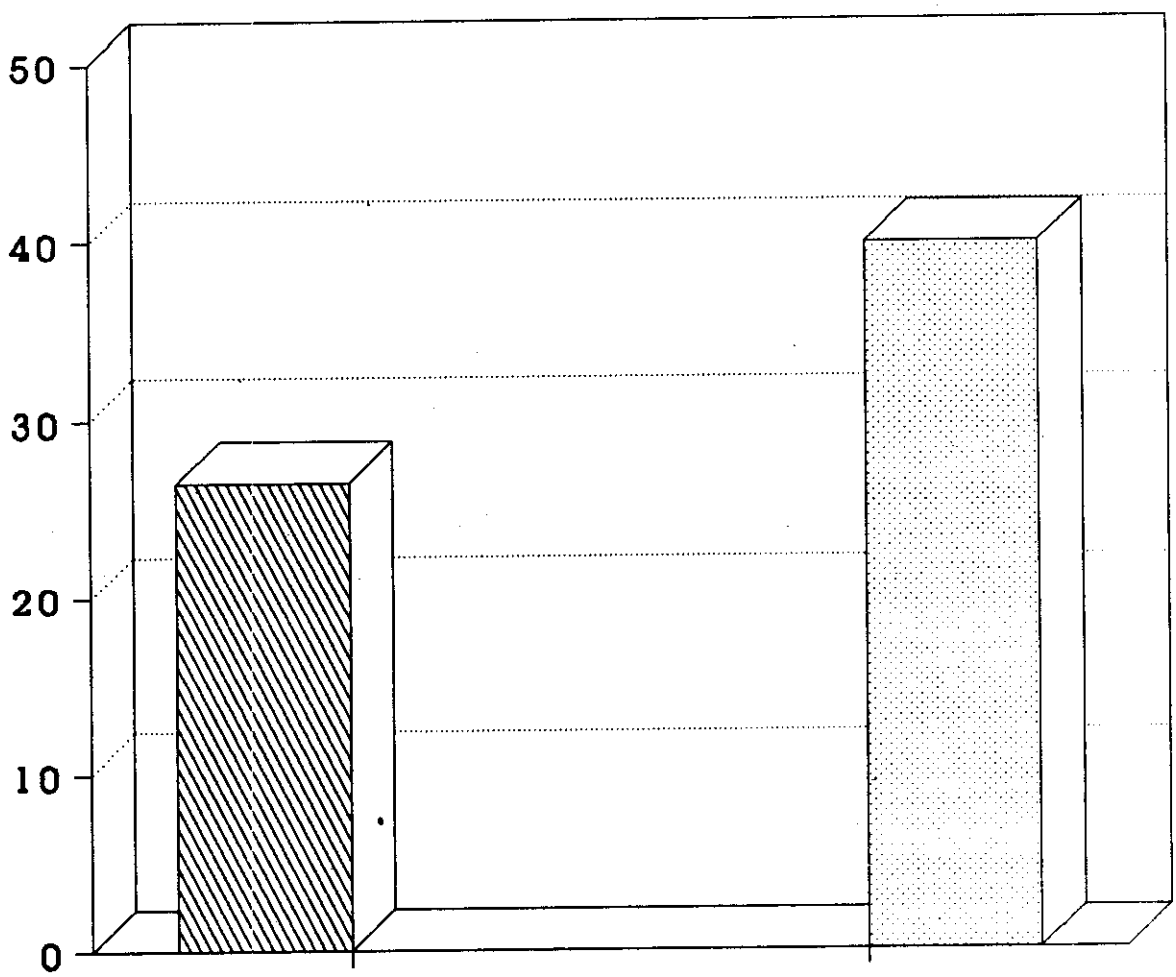
	Plasma (Fn.) mg/dl	Synovial fluid (Fn.) mg/dl
Age (years)	-0.18 *	- 0.36 *
Disease duration (years)	-0.27 *	0.33 *
E.S.R. (mm/hour)	-0.34 *	- 0.39 *
HB gm/dl	0.15*	0.15*
RBCs/mm^3	-0.2 *	0.15 *

* = P >0.05 insignificant correlation

Statistical evaluation revealed that the mean concentration of fibronectin in the synovial fluid of R.A. patients showed a highly significant elevation when compared to the mean plasma fibronectin concentration of the same patients ($P < 0.001$) **(Table 8) (Histogram 1).**

Statistical evaluation revealed that the mean concentration of fibronectin in the synovial fluid of O.A. patients showed a significant elevation when compared to the mean plasma fibronectin concentration of the same patients ($P < 0.05$) **(Table 8) (Histogram 2).**

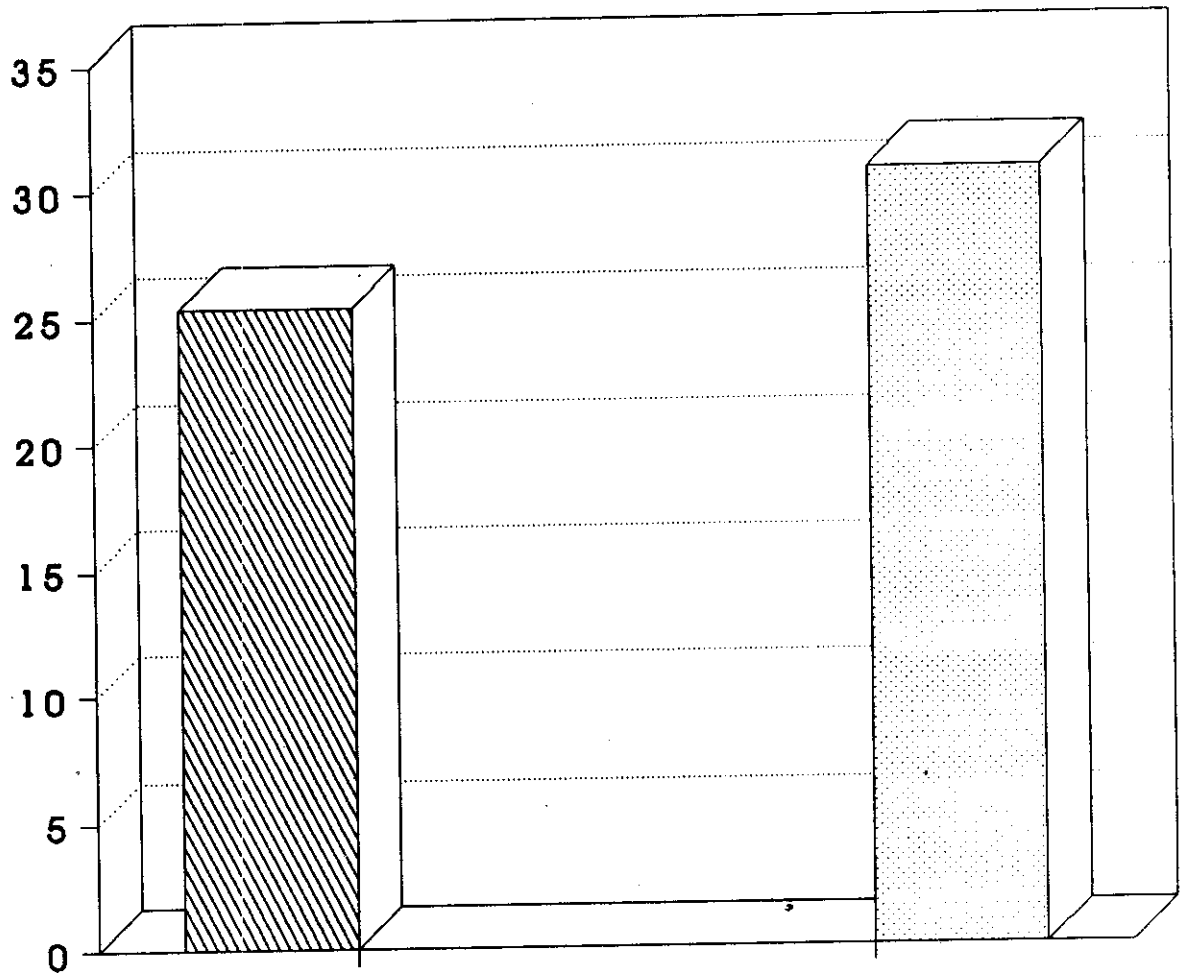
Histogram (1):



P ⟨ 0.001 = Highly significant

Comparison between the mean concentration of fibronectin in the plasma and in the synovial fluid of R.A. patients.

Histogram (2):



$P < 0.05$ = Significant

Comparison between the mean concentration of fibronectin in the plasma and in the synovial fluid of O.A. patients.

Statistical evaluation revealed that the mean concentration of fibronectin in the plasma of R.A. patients showed insignificant difference when compared to the mean concentration of fibronectin in the plasma of patients with O.A. ($P > 0.05$) **(Table 9) (Histogram 3).**

Statistical evaluation revealed that the mean concentration of fibronectin in the synovial fluid of R.A. patients showed a highly significant elevation when compared to the mean concentration of fibronectin in the synovial fluid of patients with O.A. ($P < 0.001$) **(Table 9) (Histogram 4).**

Table (9): Comparison between the mean concentration of fibronectin in the plasma of patients with R.A. and O.A., and between the mean concentration of fibronectin in the synovial fluid of patients with R.A and O.A.

	R.A. patients				O.A. patients				T	P
	N	$\bar{X}$	SD	SE	N	$\bar{X}$	SD	SE		
Plasma (FN.)	15	26.53	±6.05	±2.75	15	25.4	±5.26	±2.39	0.52	> 0.05 non-significant.
Synovial fluid (FN.)	15	39.93	±6.97	±3.17	15	30.73	±6.79	±3.08	3.5	<0.001 highly significant.

FN. = Fibronectin

N = Number of patients

$\bar{X}$ = Mean

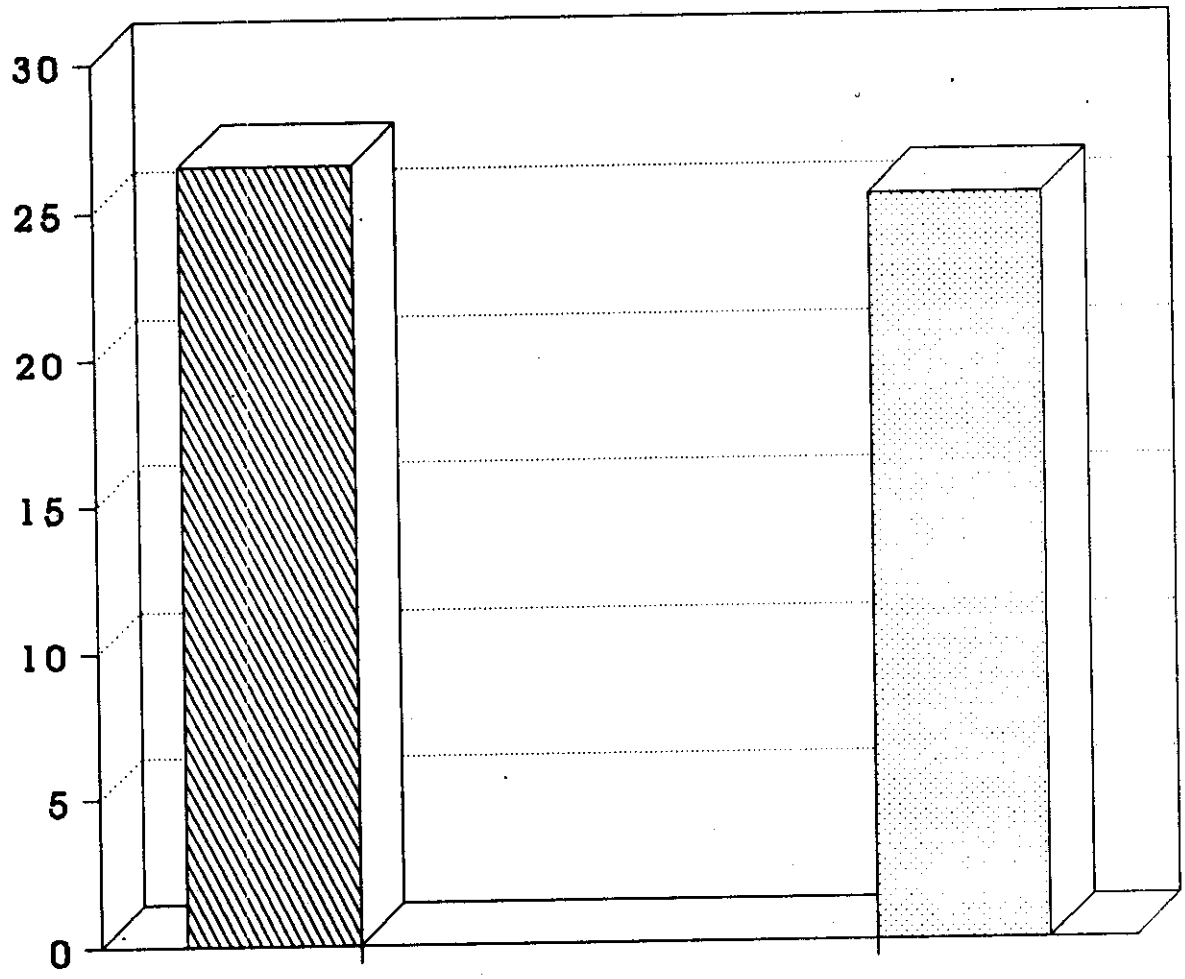
SD = Standard deviation

SE = Standard error

T = Student (T) test.

P = Probability of error

Histogram (3):



P ⟩ 0.05 = Non significant

Comparison between the mean concentration of fibronectin in the plasma of R.A. and O.A. patients.

DISCUSSION

The term fibronectin describes a family of structurally and immunologically related high molecular weight glycoproteins that are present in blood, on many cell surfaces in extracellular fluid and in connective tissues **(Mosesson and Amrani, 1980).**

The soluble form of fibronectin that can be found in blood and other body fluids has been shown to interact with the elements of haemostasis. Also it binds to fibrinogen, fibrin, sulphated proteoglycans, hyaluronic acid and components of bacterial cell wall **(Mosher, 1984).**

The insoluble (cellular) form is a component of the surface of many cells, where it has an important role in cell movement, substrate adhesion, and the maintenance of normal cell morphology and behaviour **(Yamada and Olden, 1978).**

In normal subject, the synovial fluid fibronectin concentration is about 3 times lower than that observed in the plasma **(Carnemolla et al., 1984).**

Carnemolla et al. (1984), in their study on 11 patients with R.A. using the rocket immunoelectrophoresis technique found that the mean concentration of fibronectin in the synovial fluid of R.A.patients showed a significant

elevation ($P < 0.05$) when compared to the mean plasma fibronectin concentration of the same patients.

These findings coincide with those of **Clemmensen and Andersen (1982),** who in their study on 24 patients with R.A. using the electroimmunoassay technique found that the mean concentration of fibronectin in the synovial fluid of R.A. patients showed a highly significant elevation ($P < 0.001$) when compared to the mean plasma fibronectin concentration of the same patients. They also reported that the high amounts of fibronectin in the synovial fluid of rheumatoid arthritis may originate from the blood together with other plasma proteins, as a result of damage to the fibronectin-hyaluronic acid complex by proteases and hyaluronidase enzymes. Another possible explanation is that it is derived from the degeneration of the fibronectin hyaluronic acid complex itself. A further possibility is that it is derived from the degeneration by leucocytes of fibrin with incorporated fibronectin, present where the lining cells are absent.

Lu-Steffes et al. (1982), stated that the synovial fluid fibronectin concentrations in R.A. patients were two to three times greater than the plasma fibronectin concentrations of the same patients,suggesting that either the plasma fibronectin is concentrated in the synovial

fluid or that a substantial portion of the synovial fluid fibronectin may be derived from synovial tissue cells.

These results are also in agreement with the results of **Scott et al. (1982)**, who found that the mean concentration of fibronectin in the synovial fluid of R.A. patients showed a highly significant elevation ($P < 0.001$) when compared to the mean plasma fibronectin concentration of the same patients. Using the immunofluorescent studies, they also found that fibronectin was adsorbed on the fibrinous debris in rheumatoid arthritis joints, suggesting that measurement of fibronectin levels in the synovial fluid may serve as an indicator of tissue response to rheumatoid arthritis.

McDonald et al. (1979), reported that the high concentration of fibronectin in the rheumatoid synovial fluid might also reflect the destruction of synovial tissue. Neutral leucocyte proteases are capable of degrading both fibronectin purified from human fibroblasts and the fibrillar network of extracellular, high molecular weight cell-surface fibronectin. This may lead to the loss of adhesion between cells and between cells and connective tissue, and may be an important feature in the pathophysiology of rheumatoid arthritis.

Shiozawa and Ziff (1983), have shown by the immunoelectron microscopy the presence of strong staining of fibronectin on the surface of both fibroblast-like and

macrophage-like pannus cells, suggesting that fibronectin may be produced in situ in the rheumatoid pannus.

In this work,the plasma and synovial fluid fibronectin concentrations were determined using the single radial immunodiffusion technique, we found that the mean concentration of fibronectin in the synovial fluid of R.A. patients showed a highly significant elevation ($P < 0.001$) when compared to the mean plasma fibronectin concentration of the same patients.

Carnemolla et al. (1984), in their study on 8 patients with O.A. using the rocket immunoelectrophoresis technique found that the mean concentration of fibronectin in the synovial fluid of O.A. patients showed a significant elevation ($P < 0.05$) when compared to the mean plasma fibronectin concentration of the same patients. They also reported that the peptides from thermolysin digests of fibronectin of plasma and synovial fluid, when compared on sodium dodecyl sulphate-polyacrylamide gel-electrophoresis, showed distinct differences. These data demonstrate that synovial fluid fibronectin represents a molecular form which is structurally different from that of plasma fibronectin. This suggests that synovial fluid fibronectin is locally synthesized, possibly by cell types which differ from that responsible for the production of the plasmatic fibronectin pool.

Dessau et al. (1978), reported that a loss of matrix proteoglycans can stimulate fibronectin production by chondrocytes.

Grinnell (1984), reported that increased synthesis of fibronectin by superficial zone chondrocytes in O.A. cartilage may represent part of a cellular response aiming at repair of the matrix, perhaps by stabilising local proteoglycan loss. This would be analogous to its production as part of the wound repair response in other tissues.

Dutu et al. (1986), found that the mean concentration of synovial fluid fibronectin in O.A. patients was 1.6 folds higher than the mean concentration of plasma fibronectin of the same patients.

In this study we found that the mean concentration of fibronectin in the synovial fluid of O.A. patients showed a significant elevation ($P < 0.05$) when compared to the mean plasma fibronectin concentration of the same patients.

Carnemolla et al. (1984), in their study on 11 patients with R.A. and 8 patients with O.A. found that the mean concentration of fibronectin in the plasma of R.A. patients showed insignificant difference ($P > 0.05$) when compared to the mean plasma fibronectin concentration of O.A. patients.

In this study we found that the mean concentration of fibronectin in the plasma of R.A. patients showed insignificant difference ($P > 0.05$) when compared to the mean concentration of fibronectin in the plasma of patients with O.A.

Also in this work,we found that the mean concentration of fibronectin in the synovial fluid of R.A. patients showed a highly significant elevation ($P < 0.001$) when compared to the mean concentration of fibronectin in the synovial fluid of patients with O.A.

Our findings coincide with those of **Carnemolla et al. (1984)**, who found that the mean concentration of fibronectin in the synovial fluid of R.A. patients showed a highly significant elevation ($P < 0.001$) when compared to the mean concentration of fibronectin in the synovial fluid of O.A. patients.

Our results are also in agreement with the results of **Carsons et al. (1981)**, who in their study on 13 patients with R.A. and 4 patients with O.A. using the double immunodiffusion technique found that the mean concentration of fibronectin in the synovial fluid of R.A.patients showed a highly significant elevation ($P < 0.001$) when compared to the mean concentration of fibronectin in the synovial fluid of O.A. patients.

These results also coincide with the results of **Richard et al.(1990)**, who found insignificant correlations between the plasma fibronectin concentrations and the E.S.R and the W.B.Cs in R.A. patients.

Gobel et al. (1984), in their study on 20 patients with R.A. using the nephelometric immunoassay technique found that the synovial fluid fibronectin concentrations showed a significant positive correlation with the synovial fluid WBCs count and a significant negative correlation with the synovial fluid complement levels. They suggest that the synovial fluid fibronectin concentration only serves as an indicator of inflammatory activity for the joint from which the specimen was obtained.

Lu-Steffes et al. (1982), found a significantly negative correlation between the levels of complement 3 (C3) in the synovial fluid of R.A. patients and the synovial fluid fibronectin concentrations of the same patients.