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A Study on Immunogenetical Factors as Marker of Fibrocalculous Pancreatic Diabetes

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Abstract:
Fibrocalculous Pancreatic Diabetes (FCPD), is a subset of Malnutrition Related Diabetes. At firstyoung FCPD patients were confirmed clinically for this study. By single radialimmunodiffusion technique IgG, IgA&IgM levels were measured and then lymphocytotoxicity test was performed for detection of HLA –association and compared. Our patient's allhad higher IgG and lower IgA&IgM levels indicating high infection rate and generalized PEM. They require endogenous insulin as having positive first degree familial association and predisposition to type I diabetes.

Keyword*: FCPD, Malnutrition, Immunoglobulin status,*

1. Introduction

FCPD is an uncommon form of diabetes, characterized by chronic pancreatitis of unknown origin and presence of large intra-ductal pancreatic stones. It is a subset of Malnutrition Related Diabetes Mellitus (MRDM)[4]. There is dearth of information on the prevalence of this disease in West Bengal and its clear cutaetiology was not yet fully established, though there was an almost generalized agreement on the pathological changes of pancreas in FCPD. The aetiology of FCDP was likely to be multifactorial, involving both environmental and genetic factors, but their roles were still largely unexplained. Respective reports from different states of India vary to arrive at any conclusion[2]. The absence of a consolidated idea about the causative factors of this disease, to collect further data from selective areas of west Bengal–specially the rural areas of this part of genetic plain having mixed patterns of socio-economic status lead us to investigate the problem from the angle of immunological state as well as the genetic resemblance.

2. Aims and Objectives

1. To confirm the subjects if their FCPD or not by clinical examination.
2. To get an idea about the effect of this disease on immunological status of our patients.
3. To search for familial association for genetic resemblance to IDDM.
4. To find the comparison with the other subsets of diabetes mellitus.

3. Criteria for Selection of Fcpd Patients

(According to WHO (1985) and Mohon)[11]

1. Occurrence in a tropical country.
2. Diabetes by WHO (1985) criteria.
   a) Onset within 10-30 years of age and BMI> 19Kg/M^2.
   b) Ketosis resistance under adverse conditions.
   c) Insulin requirement more than 2 Units/Kg/Day.
   d) Poor socio-economic conditions and a definite history of childhood malnutrition.
3. Evidence of chronic pancreatitis: pancreatic calculi on X-ray and USG.
4. Absence of other causes of chronic pancreatitis, i.e., alcoholism, hepatobiliary disease or primary hyperparathyroidism etc.

4. Materials and Methods

The patients under study had undergone a detailed interview to obtain their background history, before clinical observation[12].

a) Measurement of IgG, IgA levels by Malavoya, A.N[10]. for detecting immunological abnormalities. Immunoglobulins were measured by single radial immune diffusion technique where the antigen was allowed to diffuse out from wells in

the gel in which a suitable antibody was added. A ring was formed at the equivalence zone; the log of diameter of which was proportional to the conc. of antigen.

b) HLA –D locus typing by lymphocytotoxicity test (Singh. S.P.N.[14]) for detection of HLA – association. HLA-D locus typing is performed by modified lymphocytotoxicity test after separating the lymphocytes from freshly drawn blood by density gradient centrifugation.

5. Result and Discussion

5.1. Immunoglobulin Levels

Estimation of serum immunoglobulins I_gG, I_gA and I_gM of the FCPD patients showed that I_gG level was elevated in the patients, whereas I_gA and I_gM levels were decreased. The high I_gG level in our patients may party be due to associated high infection rate in them[15]. Whether the pancreatic islet cell antibody (PICA) in the form of circulating I_gG subpopulation was present in them needed another investigation. FCPD patients have a common history of Protein Energy Malnutrition and depressed levels of IgA&IgM might be a confirmation of that finding.

5.2. HLA-D Locus Typing

It was well known that both genetic as well as environmental factors were involved in the pathogenesis of diabetes mellitus[8]. Analysis of familial aggregation of the disorder suggested to be complex and consistent with polygenic inheritance[16,17].

The HLA-D locus typing of FCPD patients revealed that there was significant difference in the antigenic frequency between patient and control in the DR_3, DR_4, DRW_{52}, DRW_{53} and DQW_3 region. The relative risk for HLA-DR_2 was 8.5. This association pattern of enhanced DR_3 / DR_4 and depressed DR_2 resembled that of classical IDDM.

Previous studies provided evidence for a genetic basis of FCPD and it showed that FCPD possessed part of the genetic susceptibility to both IDDM and NIDDM[6,18]. However, since HLA association showed considerable interethnic variations, large member of patients with various ethnic groups should be studied to reach any conclusion.

6. Conclusion

Elevated IgG indicates high infection rates further investigation can confirm the contribution or PICA as circulating IgG. History of PEM might be the cause of lower IgA and IgM. High HLA-DR_3 association found in our subjects may explain the other micro vascular complications which are also at least as common in FCPD as in other primary forms.

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ANNEXURE

	FCPD (n= 60) ±SD	Control (n=60) ±SD
Ig G	1876.37±254.53	1591.3 ± 401.6
Ig A	208.65 ±45.63	226.1 ± 63.9
Ig M	123.86 ±76.46	170.8 ±8.8

Table 1: Immunoglobulin levels in FCPD patients (mg/dl)

		DR1	DR2	DR3	DR4	DRw52	DRw53	DQw1	DQw2	DQw3
Patients	n=60	20.0	40.0	60.0	40.0	32.0	70.0	90.0	20.0	70.0
Male	n=32	18.8	18.8	37.5	62.5	09.4	93.8	80.6	25.0	
Female	n=28	21.4	64.3	85.7	16.7	53.6	42.9	85.7	35.7	64.3
Control	n=40	25.0	70.0	15.0	20.0	20.0	20.0	100.0	25.0	35.0
Male	n=24	25.0	58.3	08.3	08.3	12.5	08.3	100.0	25.0	33.3
Female	n=16	25.0	78.5	25.0	37.5	31.3	37.5	100.0	25.0	37.5
Rel. riskRR		0.75	0.2	8.5	2.7	1.7	9.3	0.85	0.75	4.3

Table 2: HLA CLASS II Antigens of FCPD Patients % of individuals positive for