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SREE CHITRA TIRUNAL INSTITUTE FOR MEDICAL SCIENCES & TECHNOLOGY

TRIVANDRUM - 11

~~LIST OF PROCEDURES~~ DONE

PROJECT REPORT

NAME : FRANCIS BIMAL

PROGRAMME : D.M. CARDIOLOGY

MONTH AND YEAR OF SUBMISSION : NOVEMBER, 1993

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CERTIFICATE

I, Dr. FRANCIS BIMAL .....hereby declare that I have actually performed all the procedures listed / carried out the project under report.

Signature..... Bimal Francis.

Place : TRIVANDRUM

Name in FRANCIS BIMAL .....

Date : capital letters

Forwarded. He has carried out the minimum requirement of procedures / etc.

Signature

Head of the department

CONTENTS

PROJECT I : INTERMEDIATE TERM GRAFT PATENCY IN POST-CABG PATIENTS.

PROJECT II: CHILDHOOD ENDOCARDITIS

LIST OF PROCEDURES DONE
PROJECT REPORT

TITLE OF THE PROJECT: 1. INTERMEDIATE TERM GRAFT PATENCY IN POST-CABG PATIENTS.

NAME..... FRANCIS BIMAL

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CONTENTS

INTRODUCTION

Relief of symptoms and long-term survival are the primary goals of myocardial revascularization,[1,3-5] and they clearly correlate with patency of the bypass conduit. The patency rate of SV grafts has been the subject of multiple studies.[6 - 14] In the early postoperative period, 8-12% of grafts occlude, and in subsequent months, another 5-8% close, so that at 1 year, 12-20% of vein grafts are lost. The occlusion rate decreases substantially beyond the 1st year to an annual rate of 2%. At 5 years, the cumulative occlusion rate is 22-30%. The yearly attrition rate doubles in the next 5 years and reaches 50% at 10 years[8]. In the interim, however, important changes take place in patent grafts. Between 15% and 40% of patent grafts display irregularity and localized narrowing at 5 years.[19,20] At 10 years, half of the patent grafts show significant luminal changes that compromise the conduit[19]. This report attempts to analyze intermediate term graft patency in our post-CABG patients.

MATERIALS AND METHODS

A total of 44 CABG patients have undergone post operative angiographic evaluation in our institution. Fourteen of these patients under went- Post CABG angiographic evaluation for various reasons demanded by their clinical status.

The remaining 30 patients who under went post CABG angiographic evaluation were part of a protocol study where patients between 6 months and 5 years after surgery were motivated for restudy regardless of symptoms and TMT Status during follow up visits.

The patients studied less than 6 months and more than 5 years after CABG were excluded from the study. The patients who became symptomatic less than 3 months after CABG were excluded from the study.

Thus, 30 patients had a detailed work up including a detailed clinical history and physical examination and ECG, chest X ray, Doppler Echo cardiography and a graded exercise Treadmill test using the Bruce protocol.

The patients subsequently under went an angiographic evaluation which included an evaluation of the native coronary arteries, Coronary graft angiography and an LV angiogram. If there was failure to visualize any graft by direct cannulation, an aortic root angiography was done both on DSA and cine angiography to confirm occlusion of the graft. The follow up period was 1.5 +/- 0.9 yrs and the age ranged from 51.8 +/- 6.1 yrs all the patients were males.

The data of these 30 patients were analysed.

Statistical analysis

Initially the variables for all 30 patients were analyzed and their risk factors, functional class, TMT status and graft status were compared. Subsequently these 30 patients were divided into 2 groups of symptomatic (14 patients) and Asymptomatic (16 patients). The TMT Status, drug treatment, graft status were analysed in these two groups. Finally the patency of grafts to individual vessels and the relationship of

patency to the pre-operative flow in the vessel, size of the vessel grafted and whether the vessel grafted was infarct related was analyzed.

The variables were compared by 't' test for quantitative data and Chi square test for qualitative data. A multiple logistic regression model was created using a stepwise procedure for the different variables.

RESULTS

The clinical features and risk factor profile for all thirty patients are presented in Table I. The mean follow up was 1.5 +/- 0.9 years and the age 51.8+/- 6.1 yrs. Majority (73.3%) of the patients were smokers, 26.7% had diabetes mellites, 40% were hypertensives and 13.3% had a family history of ischemic heart disease. Surprisingly hyper cholestrolemia was present in only 13.3% of the patients.

Table II summarizes the New York heart Association functional class in the 30 patients pre and part- CABG. Pre-CABG the majority of the patients (70%) were in functional class III and IV and none of the patients were in FCI. Post surgery 53.3% of patients were asymptomatic and 30% patients were in FC II.None were in FC IV.

Table III show the tread mill status of the 30 patients. There was a significant improvement in the work load attained by the patients post CABG (6.6+/- 2.7 mets vs 9.0 +/- 2.8 mets) Table IV shows the number of grafts

received by the patients. The total number of grafts in 30 patients was 98 with a mean of 3.3 +/- 1.3 grafts per patient, 90% of the patients received between 2 and 5 grafts.

Table V shows the number of patent grafts in the 30 patients the majority (90%) of the patients had between 1 and 5 grafts patent. Two patients had none of their grafts patent.

Table VI shows the number of grafts occluded. Eleven (36.7%) patients had none of their grafts occluded i.e. all their grafts were patent.

The 30 patients were subsequently divided into two groups depending up upon their post-operative symptom status at follow-up.

Sixteen patients were asymptomatic and 14 patients were symptomatic.

Table VII and VIII compares the features of these two groups of patients.

The duration of follow-up and age were not significantly different between the two groups. However the asymptomatic patients had more number of negative TMTs (12 vs 2) and better effort tolerance on TMT. (10.4+/- 2.5 METS vs 7.1 +/- 2.2 mets; P = 0.002). Also the average number of grafts were significantly more in the asymptomatic group (4.0 +/- 1.0 vs 2.4 +/- 0.9) than in the symptomatic group (P < 0.0009).

The t - test for cholesterol, triglycerides, HDL cholesterol, smoking, DM, hypertension and family history were not significant between the two groups.

Nine of the 16 asymptomatic patients were not on any drug treatment. Seven asymptomatic patients were on single drug therapy 2 on nitrates, 4 on B-blockers and one on Ca-blocker. However, only 2 of the symptomatic patients wer on no drugs and 5 patients were on three drug regimen (nitrate, B-blocker and Ca-blocker). Four of the symptomatic patiencts were on two drug regimen. This was satistically significant P = 0.003.

Tables IV,V and VI shows the details of the grafts status between the asymptomatic and symptomatic patients. The asymptomatic patients had higher total number of grafts ($p = 0.03$) and a significantly higher number of patent grafts. However the number of occluded grafts ($P = 0.007$) were not significantly different between the symptomatic and asymptomatic group.

A multiple logistic regression model was created using a step wise procedure with the following variables - age, total number of grafts, occluded grafts, patent grafts, DM, hypertension, smoking, family history, cholesterol and triglycerides; only total number of grafts was significant at 0.05 level (OR = 12.5; 95% CL=1.04,125) between the symptomatic and asymptomatic groups.

Table IX shows the type of grafts used and their patency rates. The majority of the grafts was SVG. Seven patients received LIMA grafts. IMA had a patency of 85.7% and all 4 sequential saphenous venous grafts were patent. Overall patency was 72.5%.

Table X shows vessel wise patency of SVG grafts. The patency of the diagonal grafts was the poorest at 33.3%.

An analysis of patency with flow in the grafted vessel, size of the vessel grafted and infarct related vessel was made (Tables XI and XII). The size of the vessel was highly significant predictor of patency ($P < 0.0009$) with the occluded vessels having a diameter of 1.48 +/- 0.42 MM and patent vessels having a diameter of 1.84 +/- 0.40 MM. Majority of grafts to vessels > 2 MM were likely to remain patient (40 out of 46, $P < 0.005$).

The flow in the vessel grafted also predicted patency of the graft. TIMI 2 flow had the highest patency with 43 out of the 57 grafts being patient. ($P=0.01$)

An infarct related vessel did not significantly influence patency.

A logistic regression analysis of patency with size, flow, infarct related vessel and specific vessel grafted was done, size and flow were found to be significant. (Table XIII).

DISCUSSION AND CONCLUSION

This study was an attempt to assess the intermediate term graft patency in CABG patients, and to make a detailed analysis of the various factors that could influence the intermediate term graft patency in CABG patients.

The mean age of our patients was 51.8 +/- 6.1 yrs. this was almost similar to a recently published epidemiological study from our institute where the maximum number of cases with definite evidence of CAD was in the 55 to 64 year age group[21].

The most prevelant risk factor was smoking (73.3%). This is consistant with the very high incidence of smoking (50%) among male in the age group 35-64[21]. The incidence of hyper cholesterolemia was low (13.3%).

There was a significant improvement in the intermediate term functional class post CABG, with majority of the patients being in NYHA FC I or II

(83.3%). This is consistant with several large studies which show significant initial relief of angina in upto 95 per cent of patients with more than half of the patients remaining asymptomatic, and with a lower requirement for antianginal medication[3-5].

Relief of symptoms and long-term survival are the primary goals of myocardial revascularization and they clearly correlate with patency of the bypass conduit[19,20]. Therefore patients with more grafts patent are likely to remain asymptomatic with better relief of symptoms and on lesser amount of drugs[17]. This was clearly seen in our study which showed the asymptomatic patients to have a better work capacity when compared to symptomatic patient. (10.4 +/- 2.5 mets vs 7.1 +/- 2.2 mets; p = 0.002), to be an lesser number of drugs (p=0.003). These asymptomatic patients were shown to have better graft patency.

Out of a total of 98 grafts in our 30 patients there were 90 SVG, 7 LIMAG, 1 Bioflow and 4 of the SVG grafts were sequential. Sixty-five out of the 90 SVG (72.2%) were patent. Six out of the seven LIMA grafts

(85.5%) were patent and all the four (100%) of the sequential grafts were patent.

The patency rate of SV grafts has been the subject of multiple studies[6-14]. Sequential angiographic studies reveal significant morphological changes and the development of atherosclerosis in the SVG. In the early post operative period 8-12% of the grafts occlude, and in the subsequent months another 5-8% close, so that at 1 year 12-20% of the vein grafts are lost[12]. The occlusion rate decreases after that substantially and beyond the first year the annual attrition rate is about 2%. At 5 years the cumulative occlusion rate is 20-30%. The yearly attrition rate doubles in the next 5 years and reaches 50% at 10 years[19-20]. Several investigators report improved early patency of sequential vein grafts. But little information is available regarding late results and there are virtually no comparisons between single and sequential grafts in contemporary series[10,15].

IMA grafts have been shown to have the best effectiveness as a conduit in CABG with many studies showing upto 90% patency at 10 years[7,9].

Patients who were asymptomatic were likely to have had more grafts than the patients who were symptomatic at 1.5 yrs of follow-up. This was probably because the patients who had more number of grafts were the ones who were likely to have had more complete revascularization. Also the asymptomatic patients were more likely to have more patent grafts[16,17]. This fact is borne out by other long term studies (10-12 yrs) which show more patients to be asymptomatic if at least one graft was patent (52%) compared to only 27% of patients remaining asymptomatic if all grafts were closed[17-19]. By multivariate analysis only total number of grafts received by the patient was a statistically significant predictor of asymptomatic status of a post CABG patient. This again demonstrates the importance of attempting complete revascularization in patients undergoing CABG.

Analysis of vessel wise patency of SVG grafts showed that grafts to diagonals had only 33.3% patency at a mean of 1.5 years. This could be accounted for by the smaller size of most diagonals especially when compared to LAD which showed a patency of 75% at a mean of 1.5

years which compares with the 79% at 2 yrs in the study of Lytle et al[7].

When an analysis of patency was made with flow in the native vessel, size of the native vessel and infarct related vessel, the size of the grafted vessel was found to be very highly significant for predicting patency with the patent vessels having a size of 1.84 mm +/- 0.40 mm compared to the occluded vessels which had a size of 1.48mm +/- 0.42 mm.

In our study 48.8% of the grafted vessels were less than or equal to 1.5 mm which could account for the slightly poor patency rates (72.2% vs 80%) in our series compared to most Western Series.These data are consistant with most post CABG angiography studies which show poor patency rates of grafts to vessels less than or equal to 1.5 mm[19].

Also TIMI III flow in the grafted vessel prior to surgery was seen to be a predictor of early graft occlusion. This could probably be explained by the competitive flow in the native vessel and the graft thus reducing the effective graft flow[19].

By univariate and multivariate analysis hyper cholesterolemia and other risk factors were not predictors of graft patency in our study. This has been repeatedly borne out by many studies which have shown that hyper cholesterolemia only affects long term graft patency and its effects are more clearly seen at 10 year graft patency rates[11,20].

To conclude; graft patency rates in our study was comparable to the patency rates reported from elsewhere. At a mean of 1.5 years after CABG 72% of the SVG, 85% of the LIMA grafts and all sequential SVG were patent. By univariate analysis, post-operative symptom status correlated best with number of patent grafts and total number of grafts. Patients who had complete revascularization were likely to remain asymptomatic at follow up. By univariate and multivariate analysis the size of the vessel grafted and the flow in the grafted vessel are important predictors of patency.

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TABLE I

	FREQUENCY	PERCENT
SMOKING	22	73.3 %
DIABETES MELLITES	8	26.7 %
HYPERTENSION	12	40.0 %
FAMILY HISTORY	4	13.3 %
HYPERCHOLESTEROLEMIA	4	13.3 %

TABLE II

	PRE		POST	
	FREQUENCY	PERCENT	FREQUENCY	PERCENT
FC I	-	-	16	53.3
FC II	9	30.0	9	30.0
FC III	14	46.7	5	16.7
FC IV	7	23.3	-	-
	30	100	30	100

TABLE III

	POSITIVE	NEGATIVE	METS	RPP	NOT DONE
PRE	24(80%)	NIL	6.6+/-2.7	207+/-46	6(20%)
POST	14(46.7)	14 (46.7)	9.0+/-2.8	254+/-68	2(6.7%)

TABLE IV

TOTAL NO. OF GRAFTS

NO	ASYMPTOMATIC	SYMPTOMATIC	TOTAL	PERCENT
1	-	2	2	6.7
2	1	6	7	23.3
3	5	4	9	30.0
4	4	2	6	20.0
5	5	-	5	16.7
6	1	-	1	3.3
	16	14	30	100

P = 0.03

TABLE V
GRAFT PATENCY

NO. GRAFTS PATENT	ASYMPTOMATIC	SYMPTOMATIC	TOTAL	PERCENT
NONE	-	2	2	6.7
1	2	9	11	36.7
2	3	-	4	13.3
3	4	4	6	20.0
4	4	-	4	13.3
5	2	-	2	6.7
6	1	-	1	3.3
TOTAL	16	14	30	100

P = 0.007

TABLE VI
GRAFT OCCLUSION

NO. GRAFTS OCCLUDED	ASYMPTOMATIC	SYMPTOMATIC	TOTAL	PERCENT
NONE	8	3	11	36.7
1	3	7	10	33.3
2	5	3	8	26.7
3	-	1	1	3.3
TOTAL	16	14	30	100

P - NS

TABLE VII

t-test	ASYMPTOMATIC	SYMPTOMATIC	SIGNIFICANCE
FOLLOW UP (YRS)	1.4 + 0.5 (n = 16)	1.6 + 1.2 (n = 14)	NS
AGE (YRS)	50.9 + 4.4 (n = 16)	52.7 + 7.6 (n = 14)	NS
TMT METS	10.4 + 2.5 (n = 16)	7.1 + 2.2 (n = 12)	P = 0.002
TMT RPP	276 + 69 (n = 16)	221 + 55 (n = 11)	P = 0.03
TOTAL NO. GRAFTS	4.0 + 1.0 (n = 16)	2.4 + 0.9 (n = 14)	P = <0.0009

TABLE VIII

TMT - POST - OP

	ASYMPTOMATIC	SYMPTOMATIC
NEGATIVE	12	2
POSITIVE	4	10

TABLE IX

PATENCY	TOTAL	PATENT	PERCENT
SVG	90	65	72.2
LIMA	7	6	85.5
BIOFLOW	1	0	0
SEQUENTIAL (SVG)	4	4	100.0
TOTAL	98	71	72.5

TABLE X

VESSEL WISE PATENCY OF SVG GRAFTS

VESSEL	TOTAL	PERCENT	PATENT	PERCENT
LAD	24	26.7	18	75.0
D	12	13.3	4	33.3
OM	17	18.9	12	70.5
RAMUS	7	7.8	6	85.7
RCA	15	16.7	12	70.5
PDA	10	11.1	8	80.0
PLB	5	5.6	5	100.0
TOTAL	90	100	65	72.2

TABLE XI

FLOW	OCCLUDED	PATENT	TOTAL
TIMI 0	-	1	1 (1.1)
TIMI 1	7	5	12 (13.3)
TIMI 2	8	43	51 (56.7)
TIMI 3	10	16	26 (28.9)

P = 0.01

TABLE XII

	SIZE (mm)				MEAN (mm)
VESSEL	1.0	1.5	2.0	2.5	
OCCLUDED (25)	8	11	5	1	1.48 mm +/-0.42
PATENT (65)	5	20	31	9	1.84 mm +/-0.40
TOTAL (PERCENT)	13 (14.4)	31 (34.4)	36 (40.0)	10 (11.1)	

P < 0.005 P < 0.0009

TABLE XIII

LOGISTIC REGRESSION ANALYSIS OF PATENCY WITH SIZE, FLOW, INFARCT RELATED VESSEL & SPECIFIC VESSEL WAS DONE -

VARIABLE	COEFFICIENT B	O.R	SIGNIFICANCE
SIZE	2.330	10.327	0.0021
FLOW TIMI I/II	-0.819	0.440	0.2771
TIMI III/II	-1.650	0.190	0.0088

LIST OF PROCEDURES DONE
PROJECT REPORT

TITLE OF THE PROJECT: 2. CHILDHOOD ENDOCARDITIS

NAME ..... FRANCIS BIMAL

PROGRAMME : ..... D.M. CARDIOLOGY

MONTH & YEAR
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CONTENTS

CHILDHOOD ENDOCARDITIS

Infective endocarditis in children is uncommon. However among selected children, notably those who have congenital heart disease or those who have undergone a cardiac operation, endocarditis is a potentially lethal condition and is being increasingly recognized. The principles for the diagnosis and treatment of infective endocarditis in children are not very different from those for adults, but understanding of the several unusual features of endocarditis in children is necessary for the management of the pediatric patient with this infection.[1-3]

Few published data have estimated the incidence of pediatric endocarditis, either among normal children or among those at high risk. The usual practice in reports of case series is to express incidence as a percentage of the total admissions to a particular hospital for the period encompassed by the study.[5-8] Several authors, however, have attempted to estimate the risk for developing infective endocarditis in children with simple ventricular septal defects[6]. By assuming that all children with congenital heart disease living in Toronto would be

cared for in local hospitals, Shah and associates derived relative risk figures for this event. They concluded that an average child with a simple VSD had a lifetime risk of 12 to 13% for development of endocarditis. In a similar study Steeg and associates followed up 489 children with VSD.[7] For a child entering their study before age one year, the risk of endocarditis for the next decade of life was 3.2%. Gersony and Hayes reported cumulative risk figures for patients with pulmonary and aortic stenosis as well as those with VSD.[8] They found aortic stenosis and ventricular septal defect to be associated with a similar risk for development of endocarditis, whereas pulmonary stenosis was associated with a substantially lower risk. Those patients with a surgically repaired ventricular septal defect had a much lower risk for infective endocarditis, but the repair of aortic stenosis did not decrease the rate of subsequent infection. Overall a patient with a simple VSD treated medically had a thirty year risk of 9.7% for the development of endocarditis.

These studies provides useful perspectives on the magnitude of the problem for children with congenital heart disease. One should interpret the disease rates with caution, however, because lesions of various

severities have been considered as a single group. Because endocarditis is potentially a late complication of congenital heart disease, the relatively short periods of follow up in these studies would also introduce bias. Most other reported information has been in the form of series of clinical or autopsy cases. Although one cannot estimate risk from such data, these types of studies can provide descriptions of the natural history of endocarditis in children.

In major series done over several decades upto the early 1980's the changing pattern of etiological agents, changes in the type of prevalent heart disease and the increasing incidence of infective endocarditis overall has been stressed.[11,13] Changes in the diagnostic methods, improved survival of infants and children with congenital heart disease coincident with improved intensive care of seriously ill infants and children and improved antibiotic treatment have all resulted in a dramatic change in the clinical outcome of infective endocarditis in children in the last decade. This change has been studied in multiple reviews from the developed countries.[5,11,13]

Macaulay reported a series of 14 cases of endocarditis in children younger than two years of age in a study encompassing a 31 year period.[9] The cases were identified by a search of autopsy records and thus were fatal cases. The micro biological data was scanty; only three patients had positive cultures reported, and none of these was of valvular vegetations. Apparently only one patient had blood cultures taken. None of the patients had congenital heart disease, but many had antecedent foci of presumably bacterial infection. This study along with that of Gelfman and Levine[10] represents the pre-antibiotic experience. The latter report, also an autopsy study, described an important association between congenital heart disease and death from endocarditis.

Blumenthal and associates described pediatric endocarditis at Babies Hospital in New York City from 1930 to 1960[11] They reviewed 58 cases from that 30 year period; the ages of the patients at presentation ranged from 3 months to 14 years, and 41 patients had congenital heart disease. The most common malformations were tetralogy of Fallot (8 patients), simple Ventricular septal defect (7 patients), and patent ductus arteriosus (5 patients). Eighteen of the patients had underlying

rheumatic heart disease (1 of the 58 patients had both congenital and rheumatic lesions) most of these cases occurring in the initial 15 years of the study. Seven of their cases occurred after ligation of a PDA or creation of a systemic to pulmonary arterial shunt. The organism most frequently isolated in the study by Blumenthal and associates was viridans streptococci, noted in 38 patients. In the pre-antibiotic era, these children uniformly died. With the introduction of penicillin, however, mortality decreased sharply. Twenty children with viridans streptococcal endocarditis were treated with penicillin and all survived. Moreover, the sensitivity of the organisms to penicillin showed great stability over 15 years. The 10 patients with staphylococcus aureus endocarditis showed higher mortality despite antibiotic therapy. Five of these patients had recently had a non cardiac operation and associated wound sepsis in the post operative period; two other children had pyoderma - a finding that emphasizes the role of skin and wound infections as portals of entry for staphylococcal bacteraemia.

Zakrzewski and Keith[12] assessed the experience with pediatric endocarditis at the Toronto Hospital for Sick

children for the period of 1952 to 1962.They identified 50 children with evidence of infection, of these 45 had a congenital heart lesion; tetralogy of Fallot and ventricular septal defect were the most common. Of importance is that 13 of the 50 cases occurred after a cardiac operation. Most of these infections were caused by S. aureus, and although precise mortality figures were not available, the authors noted that these patients did poorly. They also noted that S. aureus had become the most common etiological agent for endocarditis of their institution. From 1952 to 1958 viridans streptococci has been most common, but subsequently S. aureus became predominant, followed closely by S. epidermidis. Three cases of gram negative endocarditis occurred; overall, 80% of the infections more caused by viridans streptococci, S. aureus or S. epidermidis. These authors also noted a high proportion of patients with antecedent infections of skin, bone or lung.

A large series of patients was reported by Johnson and associates[13] from the Children's Hospital Medical Center in Boston. For a 40 year period, they identified 141 patients who had one or more episodes of endocarditis. The overall survival rates steadily

increased, reaching 76% during the antibiotic era. They observed that the proportion of patients with congenital heart with congenital heart lesions increased, as did the average age of the patient. The latter could well represent increased survival of children with congenital heart disease. Only 12% of the patients had no underlying heart lesion. The most common malformation noted was tetralogy of Fallot, followed by isolated ventricular septal defect for the total group viridans streptococci was the most common pathogen, constituting 45% of the isolates. The prevalence of this organism did not change during the 40 year period. The next most common isolate was S. aureus, and this pathogen showed an increasing frequency. By the end of this study it was the causative agent in 33% of the cases.

A predominance of tetralogy of fallot was noted by Rose in an autopsy study of endocarditis in 728 children with congenital heart lesions. He found bicuspid aortic valve to be second in frequency.

A series of 11 patients was reported by Caldwell and associates[14] for the period 1964 to 1970. Nine of these children had congenital heart disease including three

with tetralogy of fallot. Three of the patients had blood cultures positive for alpha haemolytic streptococcus, three had S.aureus, two had gamma haemolytic streptococcus, two had Enterobacter aerogenes and one had a negative culture.

A further indication of the emergence of S.aureus as the predominant organism in paediatric endocarditis was evident from preliminary data obtained by the American Heart Association through a national survey of major medical centers. S.Aureus was associated with 35% of all cases of endocarditis in patients younger than age 25 years; Alpha-haemolytic Streptococci accounted for 20% of the cases.

Neonatal and Infant endocarditis is an entity distinct from endocarditis in older children. Septicemia is common in neonates, particularly premature infants, and invasive monitoring of this group of patients has become increasingly prevalent. Nevertheless, endocarditis rarely occurs in this age group. Most of the information about neonatal endocarditis has appeared in case reports. Johnson and associates[5] found 12 cases of endocarditis among 847 infants who died of sepsis. Of the total group,

61 patients had congenital heart disease, and 6 of the 12 cases of endocarditis had occurred in patients who had congenital heart disease. The authors concluded that an important association existed between cardiac infection and congenital heart lesions. The organisms isolated included B-hemolytic Streptococci (four patients) S. aureus (three patients), Streptococci not further identified (two patients), gram negative bacilli (two patients), and streptococcus pneumoniae (One patient).

There is very little data concerning infective endocarditis in children from developing countries. It is thought that in developing countries Streptococci are much more common than Staphylococci as compared to series reported from the West[2]. Kohli has published a series of 25 children with infective endocarditis[4]. Pathological data of another 16 patients who had infective endocarditis was also analysed. There were 20 cases with underlying congenital heart disease and 15 with rheumatic heart disease. Six had no pre-existing cardiac disease. Tetralogy of Fallot was the commonest congenital heart lesion and MR the commonest Rheumatic heart disease. Alpha - haemolytic Streptococcus was the most common organism closely followed by S. aureus; however

microbiological data was available in only 48 percent of cases.

In this study an attempt was made to study infective endocarditis occurring in children under 15 years of age over an eight year period.

Subjects and Methods:-

Cases were drawn from the medical records department of our Institute during the last 8 years (March 1984 to May 1992). A retrospective analysis was conducted of all records of pediatric patients with infective endocarditis. Hospital records were reviewed for clinical presentation, laboratory results and echocardiographic findings. The number and duration of antibiotics received by each patient was also noted.

Criteria for diagnosis of infective endocarditis were similar to those of Hansen and associates;[16]

Patients with previously known heart disease must fulfill at least two of the following criteria;

i) Vegetations verified by echo,
ii) Fever without any extra cardiac focus,
iii) Bacteraemia without extra cardiac focus,
iv) Symptoms compatible with embolism,
v) A new pathologic heart murmur.

Standard methods were employed for obtaining and processing blood cultures, as well as for the identification of microorganism isolates. Antibiotic susceptibility was determined by the agar dilution technique. Infective endocarditis related deaths were defined as those which occurred while the patients were under treatment for infective endocarditis or within one week of termination of treatment, unless clear clinical and pathological data suggested otherwise. Adequate antimicrobial therapy was considered as the administration for a minimum period of 14 days, of one or more antimicrobial agents with in vitro bactericidal activity against the corresponding isolate.

RESULTS:

During the 8 year study period 21 patients fulfilled the diagnostic criteria for infective endocarditis.

AGE AND SEX: Table I shows the age and sex distribution of all 21 patients;

The youngest patient was 1 1/2 years old and the oldest was 15 years of age. The mean age was 9 years. There were 11 males and 10 females.

PRESENTING ILLNESS AND DURATION:

Table II summarizes the presenting illness in the 21 patients.and table III, the duration.

Fever was the commonest presenting symptom and was present in all 21 patients. Five patients presented with progressive dyspnoea an exertion. Three patients had congestive heart failure and two patients arthralgia. Other manifestations were haemoptysis, petechiae, haematuria and haematemesis. Fever was the first

presenting symptom in all 21 patients. Duration of fever varied from 7 days to 180 days with a mean of 57 days. Majority of the patients had fever less than 1 month and 6 patients between 1 and 2 months.

UNDERLYING CARDIAC LESION:- TABLE IV Summarizes the underlying cardiac lesion in 21 cases. Congenital heart disease was the predominant underlying heart disease. VSD with or without an associated lesion was the most common cardiac lesion, followed by tetralogy of fallot and bicuspid aortic valve. Rheumatic heart disease was present in only three patients.VSD with or without associated lesion was present in 12 (57%).

ORIGIN OF SEPSIS:- The Origin of Sepsis could be identified in only four (19%) patients. Table V shows the origin of Sepsis in these four patients.

THE CAUSATIVE ORGANISM:- Table VI shows the incidence of the organisms cultured. The Causative Organism could be identified in 19 out of 21 cases (90.4%). Two cases were culture negative, those two cases had typical features of infective endocarditis including vegetations.

There was a high incidence of coagulase negative Staphylococcus in this series. However these patients had the same organism cultured on more than one culture and had other typical features of infective endocarditis including vegetations, which were present in four out of the five cases. All cases of coagulase negative endocarditis were sensitive to most antibiotics and showed at least a partial clinical response to crystalline in this group of patients with complete recovery in all 5 cases.

SITE OF VEGETATIONS :- A detailed 2-D Echocardiography revealed definite vegetations in 18 of the 21 patients (86%). In VSD the vegetations were seen in relation to the tricuspid valve, edge of the VSD, RVOT and pulmonary valve. In the case of VSD with AR the vegetations were seen on the AV and PV. In ToF the vegetation was found on the tricuspid valve. In VSD-PS on the RVOT. In Bicuspid Aortic valve on the aortic valve. In RHD the vegetation was usually present on the involued valve.

COMPLICATIONS :- Seven of the 21 patients (33%) died. The features of these patients are summarized in Table VIII. All for patients with VSD AR died. One patient with VSD, one with ToF and one patient with ToF with Waterston

Shunt died. Only one of the seven cases was culture negative there was no specific organism with an increased mortality. Five of the seven patients were more than 5 years of age. Five of the 7 deaths were secondary to some complication, and 4 of there were due to embolism, 2 due to cerebral and 2 pulmonary embolism. The complications are summarized in Table VII.

Discussion & Conclusion

Osler Originally described infective endocarditis in 1885.[17] Since then in the West there has been significant changes in the profile of patients with infective endocarditis especially in children.[1,2] Reviews from the West have drawn attention to the noteable decrease in the frequency of RHD as a predisposing factor in infective endocarditis and several series show complete disappearance of RHD as a predisposing cause.[13] In developing countries RHD is still thought to be a common predisposing cause in childhood infective endocarditis as shown in the study by Kohli and associates[4] where there was a 43% incidence of RHD as a predisposing factor in infective endocarditis, however these authors have

included children upto 18 years of age, while the present study have included cases only upto 15 years of age. There were only 3 cases of RHD out of the 21 cases which accounts for 24 %. This suggests a trend towards what has been experienced in the West, that is a steady decline in the incidence of RHD as the predisposing factor in infective endocarditis.

The increased survival of patients with congenital heart disease in developed countries, concomittant with the reduction in the incidence of rheumatic fever has resulted in an increase in the incidence of infective endocarditis an preexisting CHD. In major series from the west and in the series by Kohli etal the commonest CHD involved was TOF.[1,4,11-13] However in our series the commonest CHD was VSD with of without associated malformations (57%). TOF and Bicuspid aortic valve were the second most common lesion. However in most series TOF, VSD and bicuspid aortic valve are the three most common lesions associated with infective endocarditis.[15,16] The source of infection could be identified in only 4 out of the 21 patients (19%). However in the series by Johnson et al[5] the origin of sepsis could be identified in

only 21% and in the recent report by Paras[15] in 6 patients(26%).

Positive cultures could be obtained in 90% (19 out of 21) cases which compares well with reports from other series, which is in the range of 80 to 90%.[1,12] Paras reported culture positivity in 96% cases. In the study by Kohli etal only 48% had positive cultures. Unlike series from the West which shows a high incidence of Staphylococcus aureus endocarditis,[13] The commonest organism in this series was coagulase negative Staphylococcus, closely followed by Streptococcus viridans. The 5 cases with coagulase negative staphylococcus had cultures positive on more than one occasion and a broad spectrum of antibiotic sensitivity with at least partial response to crystalline penicillin and gentamycin. All five of these patients had complete recovery.

A predominance of males in adult series of infective endocarditis is wellknown however in younger age group females are as often involved as males both in this study and series from the West - Nadas et al.[13] However in the study by Kohli et al[4] there a marked male predominance in childhood endocarditis.

Echocardiography is an important tool in locating the infection. Echocardiograms were carried out in all the 21 patients. 18 out of the 21 (86%) patients had defenite vegetations. The series by Paras et al[15] showed an 52% incidence of vegetations demonstrated by echocardiography.

Inspite of the marked improvement in therapy infective endocarditis remains a very severe disease with a mortality of 33% (7 out of 21) in our series, which is very similar to that reported by other recent paediatric series - Paras et al - 26%. Five out of the 7 patients died due to a secondary complication and 4 out of the 5 cases were embolic. All four patients with VSD AR died, one patient with VSD, one with TOF and one with TOF and Waterston Shunt died. Unlike most other series which showed a higher mortality in younger children especially less than 2years of age[5], 5 out of the 7 patients were more than 5 years of age.

To conclude, this study shows that infective endocarditis in children in not uncommon in this country.

The clinical features, predisposing lesions and outcome of therapy of infective endocarditis are similar to what is seen in the West. Though mortality from endocarditis occurred in a slightly older age group and Saphylococcus aureus was not as common as is reported in other series.

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Table I

Age and Sex Distribution of all 21 patients

Age	Male	Female	Total
0-5	2 (9.5)	3 (14.2)	5 (23.8)
6-10	3 (14.2)	3 (14.2)	6 (28.5)
11-15	6 (28.5)	4 (19.0)	10 (47.6)
Total	11 (52.3)	10 (47.6)	21 (100.0)

The figures in bracket indicate percentages.

Table II

Clinical presentation of the 21 patients with negative blood cultures

Feature	No.of cases	%
Fever	21	100.0
Progressive DOE	5	23.8
Congestive Heart failure	3	14.2
Joint Pain	2	9.5
Haemoptysis	1	4.7
Mycotic Aneurysm	1	4.7
Petechiae	1	4.7
Haematuria	1	4.7
Haematemesis	1	4.7

Table III

Duration of Fever

Duration	No. of Cases	%
< 1 month	10	47.6
< 2 months	6	28.5
< 3 months	1	4.7
< 4 months	2	9.5
< 5 months	1	4.7
< 6 months	1	4.7

Table 1V

Underlying Cardiac Lesion

Lesion	No.of cases	%
Ventricular Septal Defect	6	28.5
Ventricular Septal Defect with aortic regurgitation	4	19.0
Tetrology of Fallot	2	9.5
Post-op Tetrology of Fallot	1	4.7
Bicuspid Aortic value	2	9.5
Rheumatic heart disease		
AR	2	9.5
MR	1	4.7
PDA	1	4.7
PDA,VSD,PAH	1	4.7
VDS,PS	1	4.7

Table V

Focus	No
Dental Caries	1
Pyoderma	1
Upper Respiration Infection	1
Otitis Media	1

Table V1

Incidence of Organisms Cultured

Organism	No.	%
Coagulase Negative Staphylococcus	5	26
Streptococcus Viridans	4	21
Staphylococcus Aureus	2	11
Streptococcus Faecalis	2	11
Pneumococcus	1	5
Non Haemolytic Streptococcus	1	5
Klebsiella Pneumoniae	1	5
Stahylococcus Albus	1	5
Salmonella	1	5
B Haemolytic Streptococcus	1	5

Table VII

Complications

Complications	No.
Pulmonary Embolism	3
Cerebral Embolism	3
Recanalization of PDA	1
Septic Pneumonitis	1
Mycotic Aneurysm (Popliteal Artery)	1
AR	1
Glomerulonephritis	1
Seizures	1
Total	12

TABLE VIII

SUMMARY OF PATIENTS WHO DIED

NO	AGE	SEX	DIAGNOSIS	VEGETATION	ORGANISM	CAUSE OF DEATH
1	11	F	VSD-AR	NIL	ALPHA-HAEMOLYTIC STREPTOCOCCUS	MASSIVE PULMONARY EMBOLISM
2	12	F	TOF-WATERSON SHUNT	AV,PV, RPA	ALPHA-HAEMOLYTIC STREPTOCOCCUS	SEVERE AR-CHF
3	10	M	VSD-AR	AV	STAPHYLOCOCCUS AUREUS	ACUTE CHF-REACTIVATION OF RHEUMATIC FEVER
4	4.5	F	VSD-AR	AV	NON HAEMOLYTIC STEPTOCOCUS	INTRACRANIAL HEMORRAGE
5	7	M	VSD	PV,LPA	PNEUMOCOCCI	PULMONARY EMBOLISM MASSIVE HAEMOPTYSIS
6	12	M	VSD-AR-PR	PV	CULTURE NEGATIVE	STATUS EPILEPTICUS PROLIFERATIVE GLOMERULONEPHRITIS
7	1.5	M	TOF	TV	KLABSIELLA PNEUMONIAE	CEREBRAL EMBOLISM