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A COMPARATIVE STUDY OF ECHOCARDIOGRAPHY AND RADIONUCLIDE 99M-TC MACROAGGREGATED ALBUMIN (MAA) SCAN IN DETECTION AND QUANTIFICATION OF REVERSAL OF SHUNT IN ACYANOTIC CONGENITAL HEART DISEASE IN CHILDREN

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ABSTRACT

Acynotic congenital heart disease is because of left to right shunt seen in Atrial Septal Defect (ASD), Ventricular Septal Defect (VSD) and Patent Ductus Arteriosus (PDA). Left to right shunt leads to Pulomonary artery hypertension (PAH) because of increased volume of flow and sheer pressure forces that combine to damage the pulmonary vasculature. Over a long time, the hyperkinetic PAH becomes fixed and leads to reversal of shunt (Eisenmenger syndrome). These congenital heart diseases are associated with better surgical outcome if timely diagnosed and operated. PAH may even come to normal baseline level and the child may live a normal healthy life if got evaluated and treated at an early stage. The current study was proposed to compare the echocardiography and 99m – TC Radionuclide scan (MAA) to detect and quantify reversal of shunt in Acynotic congenital heart disease in children.

INTRODUCTION

Congenital heart disease (CHD) is the most frequent form of major birth defects in newborns affecting close to 1% of newborn babies (8 per 1,000 live birth). As per American Heart Association, approximately 35,000 babies are born every year in the United State with some type of congenital heart disease. More deaths in the first year of life occurred due to CHD as compare to any other birth defect. Many of these defects need to be followed carefully. Some of them heal over time, but others will require treatment. Congenital heart defects are broadly classified into two categories: cyanotic and acyanotic lesions. The common cyanotic lesions are tetralogy of Fallot and transposition of the great arteries. Hypoxia is major problem than congestive heart failure in infants with cyanotic lesion. Ventricular septal defect, atrial septal defect, patent ductus arteriosus, atrioventricular canal, pulmonary stenosis, aortic stenosis and coarctation of the aorta are commonest cause associated with acynotic lesions. In infants with acyanotic lesions, congestive heart failure is the primary concern. Some infants with severe acyanotic varieties of congenital heart disease may fail to thrive and may have breathing difficulties. CHD is the common cause of morbidity and mortality. Of all CHDs, VSD is the commonest. In developing country like India, surgical repair facilities are not available to all and many patients come beyond stage of operability. Though many may not require surgery, it is important to follow up these patients before the shunt reverses in any of them at which point they become inoperable. Hence early identification of lesions which are still operable, is of paramount importance. Results of surgical repair and somatic growth after this repair from India have decidely improved with time. **Vaidyanathan B et al**[1] in 2006 reported 90 consecutive infants, followed after VSD closure at referral centre in Southern India and they studied children showed significant improvement from baseline, therefore of these children which were picked up by non invasive techniques, the outcome even in developing country seems to be promising. It is encouraging to note that age at surgery currently as reported by Vaidyanathan B et al was 7.2 ± 3.2 months. The risk of death from congenital heart disease surgery has dropped from approximately 30 percent in the 1970s to less than 5 percent in most cases today. **Engle M et al**[2] **in 1987** observed that of all the intracardiac shunts VSD is the commonest ACHD accounting for nearly 30% of all patients seen by Pediatric cardiologists with an incidence of 1.5 to 2.5 per 1000 babies.

Another study by **Park M et al**[3] **in 1996** observed that the VSD is the most common CHD, accounting for 15 to 20 percent of all cases of isolated CHD.

Van Praagh et al[4] in 1992 reported that the incidence of VSD was 20 – 25 % of all congenital heart disease.

In the pediatric age group a cardiac etiology is often responsible for secondary PAH. This is particularly important for both a diagnostic and therapeutic standpoint as many lesions are readily reparable with corrective surgery. Often PAH may be drastically reduced and returned to baseline, following corrective surgery. Early identification of the same is associated with a better surgical outcome. PAH in congenital heart diseases with a left to right shunt (ASD, VSD and PDA) are both due to increased volume of flow and sheer pressure forces that combine to damage the pulmonary vasculature. The hyperkinetic PAH becomes fixed after a span of time and is frequently complicated by shunt reversal (Eisenmenger syndrome). Once clinical manifestations become apparent with cyanosis and clubbing, the surgical outcome becomes dismal. So methods which can aid early detection can help the patient by contemplating early surgery which would be of considerable significance in a developing country like India where prioritization may help the cardiothoracic team. Echocardiography is one of the commonest and easy available technologies for the cardiac evaluation. But It has some limitation in detection of reversal of shunt. In such cases, Radionuclide scan can be more sensitive method which can be used for the evaluation of reversal of shunt, so that management of patients can be planned accordingly either medical, surgery or both.

MATERIAL AND METHODS:

After ethical committee approval the study was conducted at Maulana Azad Medical College New Delhi and its associated Lok Nayak and GB Pant Hospital, New Delhi. For radionuclide study patients were referred to Institute of Nuclear Medicine and Allied Sciences (INMAS), New Delhi.

Inclusion Criteria:

1. Children > 1 year of age
2. Large size VSD as assessed by
a) absolute size > 7 mm, and / or
b) relative size > 30 mm/m^2
3. Large PDA as assessed by Qp : Qs ratio of > 2.5

Exclusion Criteria:

1. Presence of cyanosis and clubbing (Established

Eisenmenger syndrome).
2. Primary parenchymal pulmonary disease.

Sample size :
In order to detect a reversal of shunt with an expected frequency of 60% at an 80% confidence interval 40 children were recruited for the study. Only 40 large sized VSD children were enrolled, as no case of ASD or PDA fits in the inclusion criteria during our study period of 1.5 yrs.

Children with a history of breathlessness/ respiratory distress, feeding difficulties, and feeding diaphoresis were examined clinically for evidences of a left to right shunt. All the selected children were evaluated by a clinical history, baseline spo2, chest x-ray, ECG, both 2-Dimensional and color Doppler Echocardiography and radionuclide study.

Parameters assessed by echocardiography are:
1. Absolute size of the defect.
2. Right ventricular systolic pressure and shunt across the defect.
3. Assessment of pulmonary vascular pressure.

After infusion of Radionuclide 99m-TC MAA as per standard protocol (The children were given 0.2Ci/kg of MAA tagged with 99m-Tc with a minimum dose of 500 Ci), a single whole body posterior view was taken at 5 minutes. The appearance of radiotracer in the systemic circulation was taken as an evidence of right to left shunting.

The quantification of shunts was done using the semi-quantitative method of Gates:

Total body counts- Total lung counts / Total body counts 100 = % of right to left shunt

Statistical Analysis:
All proportions were analyzed using the chi-square or Fischer's exact test and continuous parametric variables were analyzed using the student t-test. Non-parametric continuous variables have been assessed using appropriate statistical tests.

RESULT & DISCUSSION
The study population included 40 children with large sized ventricular septal defect (≥7mm) during one and half year period. During the course of the study we did not get any child with a PDA with age more than I year fulfilling the criteria. For quantification of reversal of shunt based on the semi-quantitative method of Gates , children were divided into three groups. 1st group (67.5%) having no reversal of shunt (≤ 10 %), 2nd group (17.5%) having shunt reversal of 10-20 %, & 3rd group (15%) having shunt reversal of > 20 %.

AGE DISTRIBUTION:
Most common age group in the study population was 1 – 2 year (40%) followed by 2 – 3 year age group (20% .(Table 1)

Table 1: Age distribution

Age Group (years)	No. (% of cases)
1-2	16 (40%)
2-3	8(20%)
3-4	4(10%)
4-5	2(5%)
5-6	2(5%)
6-7	2(5%)
7-8	1(2.5%)
8-9	3(7.5%)
9-10	1(2.5%)
≥ 10	1(2.5%)
Total	40

GENDER DISTRIBUTION:
27 (67.5 %) of the study population were male and 13 (32.5 %) were female. 10 (37.04%) out of 27 males and 3 (23.08%) out of 13 female children enrolled in study were detected with reversal of shunt on MAA scan.

CLINICAL FEATURES:
Most common clinical symptom present in study population was cough (95%) followed by fever (52.5%). 45% of study population had a past H/O of hospitalization. 35 patient attendants were willing for surgery. There is not significant correlation between severity of reversal of shunt and number of children presenting with cough & fever. There is not significant correlation between severity of reversal of shunt and R.D., Suck-rest-suck cycle, recurrent chest infections & requirement of decongestive measures in the past ($p<0.001$). The temporal change in symptomatology in the period just preceding the scan was not available with a definite index of reliability in the study group. (Table No. 2)

Table-2: CORRELATION OF SEVERITY OF REVERSAL AND CLINICAL PROFILE OF PATIENT WITH VSD

SEVERITY OF REVERSAL →	NO. (% OF CASES)	% OF RIGHT → LEFT SHUNT ≤ 10% (N= 27)		% OF RIGHT → LEFT SHUNT = 10-20% (N= 7)		% OF RIGHT → LEFT SHUNT > 20% (N= 6)		P VALUE
Clinical profile		No.	% of cases	No.	% of cases	No.	% of cases	
Cough	38 (95%)	26	96.2 %	6	85.7 %	6	100 %	NS
Fever	21 (52.5%)	14	51.8 %	4	57.1 %	3	50 %	NS
Respiratory distress	18 (45%)	4	13.7 %	6	85.7 %	4	66.7%	<0.001
Suck-rest-suck cycle	18 (45%)	7	25.9 %	5	71.4 %	5	83.3 %	<0.001
Feeding diaphoresis	17 (42.5%)	7	25.9 %	4	57.1 %	5	83.3 %	=0.02
Recurrent infection	17 (42.5%)	6	22.2 %	6	85.7 %	5	83.3 %	<0.001
Decongestive measures	16 (40%)	7	25.9 %	5	71.4 %	6	100%	<0.001
Past H/O hospitalization	14 (35%)	8	27.5 %	6	85.7 %	2	66.7 %	=0.01
Willingness for surgery	14 (35%)	8	27.5 %	4	57.1 %	2	33.3 %	NS

CHEST X-RAY FINDINGS:
35% of the study population had normal CXR findings in spite of having VSD. There is significant correlation between reversal of shunt and CXR findings ($p< 0.005$). As severity of reversal increased, percentage of patients with cardiomegaly, enlargement of Right ventricle (R.V.), left atrium (L.A.), left ventricle (L.V.), Pulmonary artery prominence & plethoric pulmonary vasculature increased. No patient had right atrium enlargement in CXR. As the severity of reversal increased from 10% to beyond; the skiagram evidence of RVH increased from 3.7% to 66.7%. This however cannot be used as a criteria alone in detecting reversal. (Table No. 3)

Table- 3: CORRELATION BETWEEN SEVERITY OF REVERSAL AND CXR FINDINGS

SEVERITY OF REVERSAL →	No. (% OF CASES)	PERCENTAGE OF RIGHT→LEFT SHUNT ≤ 10% (n=27)		PERCENTAGE OF RIGHT→LEFT SHUNT = 10-20 % (n=7)		PERCENTAGE OF RIGHT→LEFT SHUNT >20 %(n=6)		P VALUE
CXR Findings		No.	% of cases	No.	% of cases	No.	% of cases	
Cardiomegaly	26 (65%)	13	48.1 %	7	100 %	6	100 %	0.005

Right atrium enlargement	0 (0%)	nil	-	nil	-	nil	-	
Right ventricle enlargement	9 (22.5%)	1	3.7 %	4	57.1 %	4	66.7 %	0.0005
Left atrium enlargement	13 (32.5%)	1	3.7 %	6	85.7 %	6	100 %	<0.001
Left ventricle enlargement	26 (65%)	13	48.1 %	7	100 %	6	100 %	<0.005
Pulmonary artery prominance	12 (30%)	1	3.7 %	5	71.4 %	6	100 %	<0.001
Plethoric pulmonary vasculature	22 (55%)	10	37 %	6	85.7%	6	100	0.003

ECG FINDING:

There is significant correlation between severity of reversal of shunt detected by radionuclide scan and left ventricular hypertrophy, left atrium hypertrophy and right ventricular hypertrophy ($p<0.005$). Syamasunder Rao P et al5 in 2005, found that the electrocardiogram may be normal in very small defects or may show evidence for left ventricular hypertrophy in small to moderate defects while it may show biventricular or right ventricular hypertrophy in moderate to large defects. Left atrial enlargement sign may also be seen in ECG. Severe right ventricular hypertrophy may be seen if pulmonary vascular obstructive disease develops, that means as the severity of reversal increased, right ventricular hypertrophy dominated. Similar result have been found in our study. (Table No. 4)

Table No. – 4: CORRELATION OF SEVERITY OF REVERSAL AND ECG FINDINGS

SEVERITY OF REVERSAL →	NO. (% OF CASES)	PERCENTAGE OF RIGHT → LEFT SHUNT ≤ 10%(N=27)		PERCENTAGE OF RIGHT → LEFT SHUNT = 10-20%(N=7)		PERCENTAGE OF RIGHT →LEFT SHUNT >20%(N=6)		P VALUE
ECG findings		**No.**	**% of cases**	**No.**	**% of cases**	No.	% of cases	
Left ventricle hypertrophy	**25 (62.5%)**	12	44.4 %	7	100 %	6	100 %	0.003
Left atrium hypertrophy	**13 (32.5%)**	1	3.7 %	6	85.7 %	6	100%	<0.001
Right ventricle hypertrophy	**8 (20%)**	nil	-	4	57.1 %	4	66.7 %	<0.001
Right atrium hypertrophy	**0 (0%)**	nil	-	nil	-	nil	-	

ECHO FINDINGS :

There is significant correlation between severity of reversal of shunt detected by radionuclide scan and LAH, RVH & Pulmonary arterial hypertension ($p<0.001$). Mean pressure gradient across pulmonary valve in was 32.6 mm Hg, 50.86 mm Hg & 55.83 mm Hg in 1st group (reversal ≤10 %), 2nd group (reversal 10 -20 %) & 3rd group (reversal > 20 %) respectively . The pressure gradient across the pulmonary valve of ≥ 55 mm was a better discriminatory index and more statistically significant ($p< 0.000$) index of reversal . (Table No.5)

Table No. - 5: CORRELATION OF SEVERITY OF REVERSAL AND ECHO FINDINGS

SEVERITY OF REVERSAL →	No. (% OF CASES)	PERCENTAGE OF RIGHT → LEFT SHUNT ≤ 10% (N=27)		PERCENTAGE OF RIGHT → LEFT SHUNT = 10-20% (N=7)		PERCENTAGE OF RIGHT →LEFT SHUNT >20% (N=6)		P VALUE
ECHO findings		**No.**	**% of cases**	**No.**	**% of cases**	**No.**	**% of cases**	
Left ventricle hypertrophy	31 (77.5%)	18	66.7 %	7	100 %	6	100 %	0.06
Left atrium hypertrophy	14 (35%)	2	7.4 %	6	85.7 %	6	100 %	<0.001
Right ventricle hypertrophy	8 (20%)	1	3.7 %	4	57.1 %	3	50 %	<0.001
Right atrium hypertrophy	0 (0%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)	
Presence of pulmonary arterial hypertension	8 (20%)	0 (0%)	0 (0%)	5	71.1 %	3	50 %	<0.001

Although ECHO did not detect reversal of shunt in any child of our study, but by detecting pulmonary pressure gradient by ECHO we can predict the presence of obliterative PAH. In 12.5 percent of our cases the reversal was not affected by any discriminatory clinical, ECG or ECHO parameter and was picked up by Radionuclide scan alone, making it a superior modality for diagnosing reversal of shunt.

Malcic I and Senecic I et al[6] in 2000 found that the magnitude of left-to-right shunt in 55 children with isolated congenital heart disease [atrial septal defect (ASD) or ventricular septal defect (VSD) (muscular and perimembranous)] was estimated by two methods: radionuclide quantification and Doppler echocardiography [flow (L/min) = mean velocity x area x ejection time x heart rate].They found little difference between the magnitude of left-to-right shunt obtained with Doppler echocardiography and that with radioangioscintigraphy for a whole group of patients (N = 55, -11.42% to 12.04%) and for subgroups of ASD (n = 24, -12.49% to 12.19%) and VSD (n = 31, -10.69% to 12.23%).This study include 31 patients of VSD and 24 patients of ASD for the estimation of left to right shunt. These results indicate that both the methods are comparable. However this group did not study reversal.

Liberman L et al[7] in 2000 studied 31 patients (age 1.9 ± 1.73 years) who subsequently requiring cardiac catheterization for estimation of Pulmonary arterial pressure (PAP), the only in those patients, who had normal findings on all 4 variables, which are Doppler estimation of VSD gradient, RVH on Echo, interventricular septal orientation and VSD size, which were normal, did not have elevated PAP, but no single non invasive variable accurately predicted PAP. Patients in which 3 variables are abnormal, had elevated PAP.

We understand from the study, that conventional echocardiography may not be modality of choice to even record PAP accurately and therefore quantification and qualification of reversal of shunt prediction even be less likely. The author also conclude that prediction of PAP should be done by combination of non invasive techniques to obtain accurately predicting PAP assessment, however they did not use radio scintigraphy procedures and so, they need a new modality to assess.

RADIONUCLIDE SCAN RESULTS

Our decision to use a parameter of > 10% count is purely judgmental as there can be a error of nearly 5% due to the diffused free pertechnate and we wanted to avoid this error. No study of this kind is available in the published literature to the best of our knowledge. For quantification of reversal of shunt based on the semi-quantitative method of Gates , children were divided into three groups as described above. 1st group (67.5%) having no reversal of shunt (≤ 10 %) (Figure No. 1), 2nd group (17.5%) having shunt reversal of 10-20 %, & 3rd group (15%) having shunt reversal of > 20 %. (Table No. 6)

Table No. 6: Distribution of reversal of shunt on Radionuclide scan

Radio Scan Result	No. (% of cases)
Shunt Reversal ≤ 10 %	27 (67.5 %)
Shunt reversal > 10 – 20 %	7 (17.5 %)
Shunt reversal >20%	6 (15 %)

But Effective reversal of shunt (>10 %) found in 13 (32.5 %) patients on radionuclide scan (Figure 2). Significant correlation have been detected between severity of reversal of shunt and LAH, RVH & Pulmonary arterial hypertension ($p<0.001$).

In 8 patients, who had right ventricular dominance and PAH with pulmonary pressure gradient ≥ 55 mm Hg, demonstrated reversal of shunt on radionuclide scan, suggested that they already had gone on obliterative phase of PAH as evidenced by right ventricular hypertrophy and therefore in full blown obliterative phase, echocardiography detected reversal of shunt in such patients. However in remaining 5 patients, who had reversal of shunt detected by MAA scan, echocardiography could not detect reversal of shunt. PAH was not present in these 5 patients.

Figure No.1: MAA scan with a Left to Right shunt with No reversal with 0.5% uptake in brain

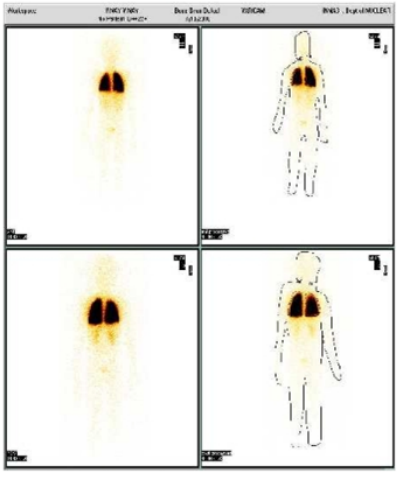
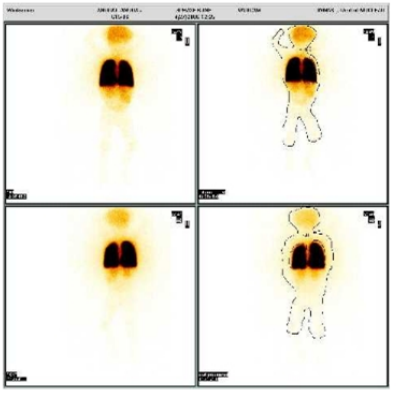


Figure No.2: MAA Scan showing a positive case of Right to Left reversal of shunt with 3.1% uptake



CONCLUSION

So we concluded from our study that Radionuclide scan by Tc-MAA is sensitive diagnostic modality for early detection of reversal of shunt in acynotic congenital heart disease patients. Every child with large size (> 7mm) VSD, must be evaluated by Radionuclide scan by Tc-MAA before planning for the surgery to predict the post surgery effect. We did not reached any conclusion in cases of ASD & PDA as no case fitted in the inclusion criteria.

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