VI. RESULTS, OBSERVATIONS AND DISCUSSION

The results of the present study are presented and discussed in accordance with the two major groups studied.

I. EPIDEMIOLOGICAL STUDY

This section pertains to the results of the epidemiological study which include -

A. Baseline survey

B. Follow up survey

II. SEROLOGICAL STUDY

This section presents the results of variables studied to determine the optimum age for measles vaccination discussed under the following heads -

A. Maternal vs. cord blood study

B. Waning of passive measles antibody study

C. Seroconversion study

Discussion follows each section and/or each head.

I. EPIDEMIOLOGICAL STUDY

A. Baseline Survey

Demographic data

In the present study, a house-to-house survey of 1754 families was conducted between 1st and 15th January, 1983 and the follow up survey between 1st and 15th February, 1983.

A total of 1754 families were covered yielding a population of 8220, the average family size being 5.2. Out of the total population, 19.23% (1581) were in the 0-6 year age group. During baseline survey, a point prevalence of 12.65% (200 cases) of measles was recorded.

Table-4 and Table-5 show the percent distribution of 1581 children (0-6 years) according to age, sex and vaccination status for BCG and measles. Of this child population, 20.30% were below the age of 1 year, 59.33% were between 1 and 4 years of age, while the remaining 20.37% were between 4 and 6 years of age. In all the age groups, the number of females was slightly higher than that of males. There were 47.49% male and 52.51% female children. The male to female ratio was 0.9. Measles vaccination coverage (2.85%) was poor as compared to BCG vaccination coverage (74.45%). It was 5.6% in the 0-1 year age group and only 2.87% in the 1-4 years age group in contrast to BCG vaccination coverage of 67.91% and 73.88% respectively.

Table-6 demonstrates the association between sex and nutritional status of children under study at baseline survey. Higher percentage of female children were malnourished (16.82%) as compared to their male counterparts (10.88%). This sex difference was statistically significant ($P \leq 0.001$). After stratifying for age, this difference was found to be significant ($P \leq 0.001$) in the age group 1-4 years. In the remaining two age groups (0-1 year and 4-6 years), a similar trend was observed which failed to reach statistical significance.

Table-7 depicts the percent distribution of children with measles according to their age and sex at baseline. Out of 200 cases identified, 18.50% were under the age of 1 year, 67.00% were in the age group of 1-4 years and the remaining 14.50% were above the age of 4 years. Thus, a total of 85.50% of children (0-6 years) suffering from measles were below

TABLE-4

PERCENT DISTRIBUTION OF CHILDREN (0-6 YEARS) ACCORDING TO AGE AND SEX AT BASELINE

Sex	Age (years)			Total	M/F
	0-1	1-4	4-6		
Male	9.48 (150)	28.78 (455)	9.23 (146)	47.49 (751)	
					0.9
Female	10.82 (171)	30.55 (483)	11.14 (176)	52.51 (830)	
Total	20.30 (321)	59.33 (938)	20.37 (322)	100.00 (1581)	

Total percent distribution
Figures in parentheses indicate number of subjects.

TABLE-5

PERCENT DISTRIBUTION OF CHILDREN (0-6 YEARS) ACCORDING TO AGE AND VACCINATION COVERAGE FOR MEASLES AND BCG

Vaccine	Age (years)			Total
	0-1	1-4	4-6	
Measles	5.60 (18/321)	2.87 (27/938)	-	2.85 (45/1581)
BCG	67.91 (218/321)	73.88 (693/938)	82.60 (266/322)	74.45 (1177/1581)

Subgroup percent distribution
Figures in parentheses indicate number of subjects vaccinated (numerator) and total number of subjects in the subgroup (denominator); percentages shown are for the same subgroup.

TABLE-6

ASSOCIATION BETWEEN SEX AND NUTRITIONAL STATUS[a] OF CHILDREN (0-6 YEARS) AT BASELINE

Age group (years)	Sex	Nutritional status[a] 0+I	II+III+IV	Chi-square value
0-1	Male	7.46 (118)	2.02 (32)	2.26 - N.S.
	Female	7.72 (122)	3.10 (49)	
1-4	Male	20.62 (326)	8.16 (129)	19.17***
	Female	17.71 (280)	12.84 (203)	
4-6	Male	8.54 (135)	0.70 (11)	0.02 - N.S.
	Female	10.25 (162)	0.89 (14)	
Total	Male	36.62 (579)	10.88 (172)	16.47***
	Female	35.68 (564)	16.82 (266)	
Total sample population		100.00 (1581)		

Total percent distribution
(a) = As per IAP Classification (Annexure : 2)
Figures in parentheses indicate number of subjects.
N.S. = Not significant
*** = Significant at $P \leq 0.001$

TABLE-7

PERCENT DISTRIBUTION OF CHILDREN (0-6 YEARS) WITH MEASLES

IN RELATION TO THEIR AGE AND SEX AT BASELINE

Age group (years)	Sex		Total
	Male	Female	
0-1	10.50 (21)	8.00 (16)	18.50 (37)
1-4	36.00 (72)	31.00 (62)	67.00 (134)
4-6	8.00 (16)	6.50 (13)	14.50 (29)
Total	54.50 (109)	45.50 (91)	100.00 (200)

Total percent distribution
Figures in parentheses indicate number of subjects.

the age of 4 years. Of the total infants suffering from measles, 10.81% were below the age of 6 months. The youngest child to suffer was a 5 month old female.

These figures are comparable with those reported by various investigators (13,22,26,75,137,191,243,263,285,295,303). In these studies, the percentage of children under the age of 4 years suffering from measles ranged from 64.00 to 86.00.

As observed by Assad (13), in the developing countries, 10-15% of the cases of measles occur during the first year of life and the highest incidence of the disease is seen in the second year of life. The young age at onset has been attributed to the large family size which provides a much greater opportunity for the spread of droplet infection. Also, the practice of carrying children by their mothers or elder sisters increases the chances of contact with other infected children.

About 55% of the cases reported by Biviji et al (26) and Silhar and Maru (303) were under 2 years of age. Lobo et al (191) have reported an incidence of 14.60% and 43.70% in the 1 year and 1-2 years age groups respectively. Bhaskaram et al (22) have reported an incidence of 21.30% and 29.50% in the 0-1 year and 1-2 years age groups respectively. Various other investigators have reported an incidence of measles in infants ranging from 15-30% (71,100,305).

Occurrence of measles in early infancy, as observed in the present study, has been earlier reported by various investigators (22,99,164, 305,316,349). Nearly 50% of cases in infancy are reported before 9 months of age (22,164,316). In a study by Sinha (305), 11.59% cases of measles in the 0-1 year age group were under 6 months of age. Bhaskaram et al

(22) have reported 34.80% of affected infants between 4 and 9 months of age and no case under the age of 3 months. In a WHO collaborative study in Kenya (349), the earliest cases of measles were seen at 5 months of age.

One of the three major factors which has to be considered while determining the earliest possible age for measles vaccination is the incidence of measles infection in the early months of life (349). In general, infants are more likely to experience complications of measles (4,13,139,160,164,308,316). It is noteworthy that measles at an early age is common in children in whom SSPE later develops. In SSPE patients in South Africa, as reported by Kipps (165), 43% had measles before the first birthday. Measles occurred in 46% of such patients in USA and 48% in UK before their second birthday (165, 242).

The high incidence of measles in infancy necessitated the study on fall in maternal measles antibody titre and efficacy of measles vaccination at less than 9 months of age (Serological Study).

Table-8 depicts the percent distribution of children (0-6 years) suffering from measles in relation to their age and nutritional status at baseline. The proportion of malnourished children was found to increase with the increase in age, although the difference was statistically non-significant.

Table-9 shows the mean age of onset of measles in children (0-6 years) after stratifying for age and sex.

The mean age of occurrence of measles was 9.3 and 9.9 months in males and females respectively in the 0-1 year age group. In the 1-4 years age group, it was 28.4 and 26.8 months in males and females respectively. In the age group of 4-6 years, it was 70.2 and 72.0 months in males and females respectively.

The age of onset of measles was similar in both the sexes in all age groups.

TABLE-8

PERCENT DISTRIBUTION OF CHILDREN (0-6 YEARS) WITH MEASLES IN RELATION TO THEIR AGE AND NUTRITIONAL STATUS [a] AT BASELINE

Group	Age group (years)	Nutritional Status [a]		Chi-square value
		0+I	II+III+IV	
a	0-1	64.87 (24)	35.13 (13)	a vs. b 1.10 - N.S.
b	1-4	55.22 (74)	44.78 (60)	b vs. c 0.22 - N.S.
c	4-6	51.72 (15)	48.28 (14)	
	Total	56.50 (113)	43.50 (87)	

Row percent distribution
(a) = As per IAP Classification (Annexure : 2)
Figures in parentheses indicate number of subjects.
N.S. = Not significant

TABLE-9

MEAN AGE OF ONSET OF MEASLES IN CHILDREN (0-6 YEARS) STRATIFIED FOR AGE AND SEX AND ITS COMPARISON IN VARIOUS AGE GROUPS AT BASELINE

Age group (years)	Sex	n	Age (months) Mean ± S.E.	't' test value
0-1	Male	21	9.3 ± 0.46	0.81 - N.S.
	Female	16	9.9 ± 0.58	
1-4	Male	72	28.4 ± 1.20	0.91 - N.S.
	Female	62	26.8 ± 1.30	
4-6	Male	16	70.2 ± 2.42	0.51 - N.S.
	Female	13	72.0 ± 2.55	

N.S. = Not significant

Beliefs and perceptions regarding causation of measles

In the management of measles, the parental beliefs and attitudes are of significant importance but are given little or no consideration. Failure to know and understand the attitudes and beliefs of the community limits effective care and increases the severity of the disease (199). The result is that the treatment given for the disease is as varied and diverse as the religious taboos and attitudes prevailing in the community.

In the present study, as shown in Table-10, 83.5% of the parents attributed measles to a divine visit of the 'Mata' or Goddess and none thought it to be a viral disease!

In India, in many rural areas, religious fatalism persists and makes effective control action against measles more difficult (68).

In most areas of India, it is generally believed that measles and other similar febrile illnesses with exanthematous lesions e.g. chickenpox, german measles, etc, are caused by a Goddess or her sisters, 'Mata' in the north and 'Mariammai' in the south (296).

In a study by Kantharia (150), 63.11% of the parents did not know the cause of measles and attributed it to a divine visitation.

B. Follow Up Survey

Out of 200 cases of measles identified at baseline, 185 could be contacted during follow up after 4-6 weeks.

Rituals observed by families during measles

Table-11 depicts the rituals observed by families during measles. The majority of families followed various rituals based on their superstitious beliefs. Of these, 87.57% families believed in visiting temple of 'Mata', while 18.92% families believed in offerings and/or prayers to appease 'Mata'.

Shah et al (296) have reported the use of charms and 'mantras' by most people to appease 'Mata' during an attack of measles.

TABLE-10

BELIEFS AND PERCEPTIONS OF RESPONDENTS REGARDING CAUSATION OF MEASLES AT BASELINE

Beliefs	n	%
'Mata' visitation	167	83.50
Body heat	9	4.50
Infectious disease	3	1.50
Viral disease	0	0.00
Do not know	21	10.50
Total	200	100.00

TABLE-11

RITUALS OBSERVED BY FAMILIES DURING MEASLES AT FOLLOW UP

Rituals	n	%
Temple visit	162	87.57
Offering/prayers	35	18.92
Nothing particular	17	9.19

Percent distribution of 185 subjects at follow up

Measles complications and treatment

Table-12 describes the complications of measles recorded during follow up visit. The majority of children (84.32%) developed complications after an episode of measles. A total of 281 complications with an average of 1.74 complications per child (281/156) were recorded. Bronchopneumonia alone or with other complications (78.38%) was the most common complication reported. The second most common complication was diarrhoea alone or with other complications (55.13%). Otitis media affecting one or both ears was observed in 10.27% of children. No case fatality was observed. However, no information concerning the fate of the 15 children missing since the first visit could be obtained. Five cases, 4 with broncho-pneumonia and one with diarrhoea, were hospitalised.

The contrast between the developed and developing worlds is most marked in relation to the severity and outcome of measles (13).

Bronchopneumonia as a most common complication of measles has been earlier reported (58,75,100). Chaudhary et al (58), Dixit et al (75) and Ghosh and Dhatt (100) reported 69.90%, 61.70% and 84.40% cases of bronchopneumonia respectively.

Diarrhoea as a complication of measles has been reported in 76% cases by Nigam et al (206). Krishnamurthy and Anantharaman (170), in a prospective study of 1000 cases of measles in Madurai, reported 39% of measles cases suffering from diarrhoea. Shah et al, in a study from Aurangabad, have reported a 22% incidence of gastroenteritis and 14% of respiratory complications following measles (296). Basu (19), in a multicentric study, reported an incidence of 50% for respiratory complications and 25% for diarrhoea. Chaudhary et al (58), in a hospital-based study, observed an incidence of 34.80% for diarrhoea and 12.10% for laryngitis.

On the other hand, in many developed countries, the participation of people in measles vaccination campaign is poor as the disease is no longer feared due to almost no complications (268).

TABLE-12

COMPLICATIONS OF MEASLES OBSERVED IN CHILDREN (0-6 YEARS) AT FOLLOW UP

		n	%
(A)	Total sample population	185	100.00
	No complication	29	15.68
	With complications	156	84.32
	Hospitalisation	5	2.70
	Case fatality	0	0
(B)	Complications recorded		
	Bronchopneumonia	57	30.81
	Bronchopneumonia with other complications	88	47.57
	Diarrhoea	15	8.11
	Diarrhoea with other complications	87	47.02
	Otitis media	19	10.27
	Others	15	8.11
	Total	281	

Table-13 depicts the percent distribution of the complications due to measles as per the nutritional status of children at baseline. The average rate of complications per child was higher in the 0-1 year age group (1.68) as compared to that observed in the 1-4 years (1.47) and 4-6 years (1.48) age groups. In general, the rate of complications per child in malnourished children was higher than that in well nourished children in all the age groups. However, on statistical analysis, this trend failed to reach significant levels.

As discussed earlier, infants are more likely to experience complications following measles (22,164,316).

The synergic detrimental effect of malnutrition and measles is important, for both contribute to an impairment in cellular immunity and so more complications are seen in malnourished children suffering from measles (13).

In view of the high incidence of measles-related complications during infancy, especially in malnourished children, it becomes imperative to attempt to vaccinate all infants in the developing countries during the narrow interval or 'window' between the loss of maternal antibody protection and the ability of infants to adequately respond to the measles vaccine, before they acquire the natural disease.

This prompted the inclusion of 6-8 months old infants in the present study on seroconversion following measles vaccination.

Table-14 depicts the percent distribution of children (0-6 years) suffering from measles, stratified for nutritional status at baseline (1) and at follow up (2).

At follow up, the percentage of children in the malnourished group (PEM grades II + III + IV) increased as compared to baseline (49.33% vs. 42.16%). However, this difference was statistically not significant. Similar results were obtained when comparisons were made within subgroups after the children (0-6 years) were stratified into the 0-1 year (41.94%

TABLE-13

DISTRIBUTION OF COMPLICATIONS OF MEASLES AS PER NUTRITIONAL STATUS[a] AT BASELINE OBSERVED IN CHILDREN (0-6 YEARS) RECORDED AT FOLLOW UP

Age (years)	Nutritional status[a]	Complications				Total per subject	Chi-square value
		Broncho pneumonia	Diarrhoea	Otitis Media	Others		
0-1	a. 0+I (21)	15	13	-	-	52	a vs. b
(31)	b. II+III+IV (10)	09	09	05	01	1.68	1.55 - N.S.
1-4	a. 0+I (72)	56	36	06	05	192	a vs. b
(129)	b. II+III+IV (47)	46	33	05	05	1.47	0.15 - N.S.
4-6	a. 0+I (14)	09	05	-	02	37	a vs. b
(25)	b. II+III+IV (11)	10	06	03	02	1.48	0.96 N.S.

(a) = As per IAP Classification (Annexure : 2)
Figures in parentheses indicate number of subjects.
N.S. = Not significant

TABLE-14

PERCENT DISTRIBUTION OF CHILDREN (0-6 YEARS) SUFFERING FROM MEASLES STRATIFIED FOR NUTRITIONAL STATUS[a] AT BASELINE(1) AND AT FOLLOW UP(2)

Age group (years)	Visit	Nutritional status [a] 0+I	II+III+IV	Chi-square value
0-1 (31)	1	67.74 (21)	32.36 (10)	0.56 - N.S.
	2	58.06 (18)	41.94 (13)	
1-4 (129)	1	55.81 (72)	44.19 (57)	1.00 - N.S.
	2	49.61 (64)	50.39 (65)	
4-6 (25)	1	56.00 (14)	44.00 (11)	0.72 - N.S.
	2	44.00 (11)	56.00 (14)	
Total (185)	1	57.84 (107)	42.16 (78)	2.14 - N.S.
	2	50.27 (93)	49.73 (92)	

Row percent distribution
(a) = As per IAP Classification (Annexure : 2)
Figures in parentheses indicate number of subjects.
N.S. = Not significant

vs. 32.26%); 1-4 years (50.39% vs. 44.19%) and 4-6 years (56.00% vs 44.00%) age groups.

Table-15 describes the mean change in weight of children (0-6 years) from baseline (1) to follow up (2) after an episode of measles. Usually, the affected children experience a marked loss of weight from both diarrhoea and the inability to eat and drink because of severe stomatitis and general malaise.

A consistent decrease in mean weight after an episode of measles was observed in all the three age categories. These decreases were not significant in the 0-1 year (6.60. kg vs. 6.20 kg) and 4-6 years (13.30 kg vs. 13.10 kg) age groups. However, in the 1-4 years age group, this difference (9.50 kg vs. 8.70 kg) was statistically significant ($P \leq 0.05$).

It is evident from Table-14 and Table-15 that malnutrition was most prevalent in the 1-4 years age group and the post-measles loss of weight was also maximum in the same age group. This further substantiates the synergic detrimental effect of malnutrition and measles.

There are several reports suggesting the adverse effects of measles on the nutritional status (141, 167, 170, 231, 234). In a series followed by Krishnamurthy et al (170), nearly 40% of the children developed grade III malnutrition following measles. Morley (231) has reported that after measles, 66% children lost 5% weight and 15% children took over 3 months to regain their previous weight. However, studies by John et al (141) and Koster et al (167) give more emphasis to availability of health care facilities and nursing care during illness in determining the course and outcome of measles rather than the nutritional status.

Table-16 reveals the percent distribution of and time interval taken for medical treatment by children (0-6 years) suffering from measles, recorded at follow up. Medical treatment was taken by 36.23% (67/185) children only. Of these, only one child took medical treatment within seven days of onset of the disease. The majority of children (86.57%) took treatment between 7 and 14 days. Even in the children who required hospitalisation, most were taken to the hospital only after 7 days.

TABLE-15

MEAN CHANGE IN WEIGHT OF CHILDREN (0-6 YEARS) FROM BASELINE (1) TO FOLLOW UP (2) AFTER AN EPISODE OF MEASLES

Age group (years)	Visit	Weight (kg) Mean ± S.E.	't' test value	Mean weight loss (%)
0-1	1	6.60 ± 0.21	0.87 N.S.	6.05
	2	6.20 ± 0.41		
1-4	1	9.50 ± 0.20	2.98*	8.42
	2	8.70 ± 0.18		
4-6	1	13.30 ± 0.41	0.35 - N.S.	1.50
	2	13.10 ± 0.39		

N.S. = Not significant

* = Significant at $P \leq 0.05$

TABLE-16

PERCENT DISTRIBUTION OF AND TIME INTERVAL TAKEN FOR MEDICAL TREATMENT BY CHILDREN (0-6 YEARS) SUFFERING FROM MEASLES RECORDED AT FOLLOW UP

Description	n	%
Total cases of measles	185	100.00
Treatment taken	67	36.23
Time interval before treatment taken		
< 7 days	1 (1)	1.49 (1.49)
7-14 days	58 (4)	86.57 (5.97)
> 14 days	8	11.94
Total	67 (5)	100.00 (7.46)

Figures in parentheses indicate number/percentage of subjects hospitalised.

In a similar study by Silhar and Maru (303), patients were given treatment only during the second or third week. In a study by Kantharia (150), 70% of measles cases were not given any treatment as it was a tradition not to do so during measles.

Shah et al, during their survey in rural India, observed that although 43% of the people took medical treatment, it was only when some complications had developed which had failed to subside (296).

To sum up, the results of the Epidemiological Study highlighted the following points-

1. The point prevalence of measles was 12.65%.
2. The measles vaccination coverage was only 2.85%.
3. Malnutrition was higher in females as compared to males in all the age groups, it being significantly higher in the 1-4 years age category.
4. None of the respondents attributed measles to viral infection, while the majority believed it to be a divine visitation.
5. Detrimental effect of measles on the nutritional status was observed; and significant weight loss was seen in the 1-4 years age category.
6. Superstitious rituals were followed by a majority of respondents and only a few cases were taken for medical attention; that too after 7 days of illness.
7. The rate of post-measles complications was higher in the malnourished children in all the age groups and was maximum in the 0-1 year age group (Fig. 8).
8. Bronchopneumonia (78.38%) and diarrhoea (55.13%) were the two commonest complications observed following measles (Fig.8).

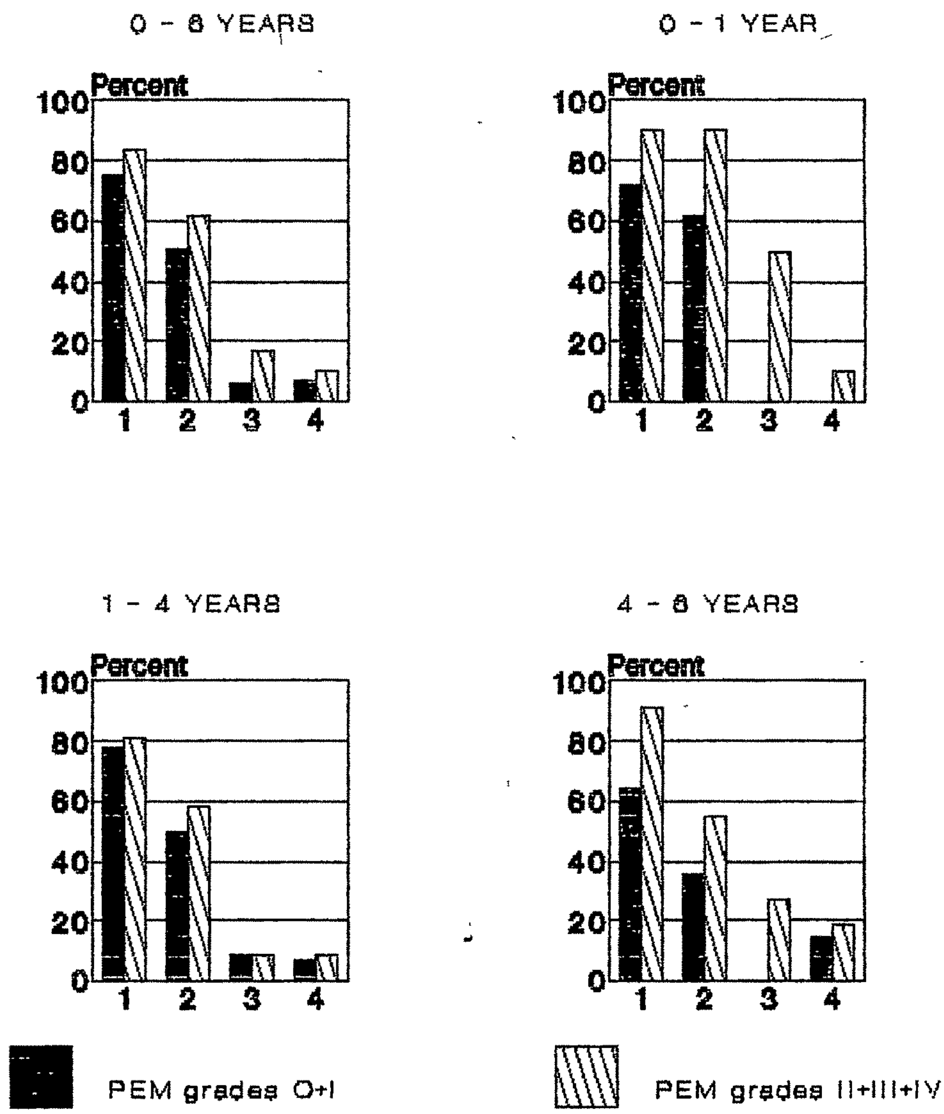
II. SEROLOGICAL STUDY

A. Maternal vs. Cord Blood Study

A total of 187 paired i.e. maternal and their respective cord blood samples were analysed. As shown in Table-17, there were 50.80% male and

FIGURE-8

INCIDENCE OF POST-MEASLES COMPLICATIONS AS PER NUTRITIONAL STATUS (@) IN VARIOUS AGE GROUPS OBSERVED AT FOLLOW UP IN CHILDREN (0-6 YEARS)



1 - Bronchopneumonia 2 - Diarrhoea 3 - Otitis media 4 - Others

(@) - As per IAP Classification (Annexure-2)

TABLE-17

PERCENT DISTRIBUTION OF NEWBORNS IN RELATION TO SEX AS PER THEIR BIRTH WIEGHT AND MATURITY [(a)]

Type	Sex		Total
	Male	Female	
FTAGA	41.18 (77)	39.57 (74)	80.75 (151)
FTSGA	4.81 (9)	4.81 (9)	9.62 (18)
PTAGA	3.21 (6)	2.68 (5)	5.89 (11)
PTSGA	1.60 (3)	2.14 (4)	3.74 (7)
Total	50.80 (95)	49.20 (92)	100.00 (187)

Total percent distribution
(a) = As per Dubowitz's classification **(79)**
FTAGA = Full term appropriate for gestational age
FTSGA = Full term small for gestational age
PTAGA = Preterm appropriate for gestational age
PTSGA = Preterm small for gestational age
Figures in parentheses indicate number of subjects.

49.20% female newborns. As per their birth weight and maturity, the newborns were designated to various subgroups –

-	Full term	- FT
-	Full term appropriate for gestational age	- FTAGA
-	Full term small for gestational age	- FTSGA
-	Preterm	- PT
-	Preterm appropriate for gestational age	- PTAGA
-	Preterm small for gestational age	- PTSGA

Table-18 depicts the percent distribution of and the correlation between maternal (M) and cord blood (F) measles HAI antibody titres.

Out of 187 cord blood samples, 6.42% had no detectable levels of passive measles HAI antibody, suggesting their probable susceptibility to measles in the newborn period. Similarly, 5.35% of maternal blood showed absence of measles HAI antibody.

The majority (83.42%) of mothers had titre values ranging from 1:4 to 1:32 and a similar finding (86.10%) was noticed in the cord blood samples also.

A highly significant correlation ($P \leq 0.001$) was observed between maternal and cord blood antibody titres.

Earlier studies by various investigators have also reported absence of measles HAI antibody in newborns (72,140,199,219). Dholakia (72) from Vadodara reported absence of measles antibody in 5.7% of newborns. A seronegativity at birth of 10% by Man Mohan et al (199), 17% by John and Jesudoss (140) and 30% by Mehta et al (219) has been reported. However, Bhaskaram et al (22), Vasani (334) and a WHO study from Kenya (349) have reported a 100% seropositivity at birth.

A significant correlation between maternal and cord blood levels observed in the present study has also been reported by Kaur et al (157), Man Mohan et al (199), Vasani (334) and a WHO study from Kenya (349).

TABLE-18

PERCENT DISTRIBUTION OF AND CORRELATION BETWEEN

MATERNAL (M) AND CORD BLOOD (F) MEASLES HAI ANTIBODY TITRES

Titre	Percent distribution		Correlation levels
	Maternal blood(M)	Cord blood (F)	
<1:2	5.35 (10)	6.42 (12)	
1:2	6.95 (13)	5.34 (10)	
1:4	17.11 (32)	21.39 (40)	
1:8	27.27 (51)	23.53 (44)	M vs F
1:16	19.25 (36)	23.53 (44)	r = 0.49
1:32	19.79 (37)	17.65 (33)	't' = 7.66 ***
1:64	3.21 (6)	2.14 (4)	
1:128	1.07 (2)	-	
Total	100.00 (187)	100.00 (187)	

Column percent distribution
Figures in parentheses indicate number of subjects.
*** = Significant at $P \leq 0.001$

The titre of maternal passive protection transmitted transplacentally to the newborn is an important factor that determines the optimum age for measles vaccination. Infants whose mothers have lower levels of measles antibody are more likely to seroconvert to measles vaccination at a younger age (349, 356).

Antibody titres following measles immunisation are much lower than those following the natural disease (242), but a rapid anamnestic response on exposure to measles virus offers a probable lifelong protection. However, when the immunised female infants grow up and have children, their lower antibody levels could cause them to pass lower levels of transplacental immunity to their children and thus make them susceptible to measles infection at a younger age. Thus, in highly immunised populations of the future, unless there is a world-wide elimination of measles, a higher number of measles seronegative newborns may necessitate measles vaccination in early infancy.

Table-19 describes the comparison between maternal (M) and cord blood (F) measles HAI antibody titres (GMT) in relation to the maturity and birth weight of the newborns.

No significant difference was observed in the levels of antibody between maternal and cord blood samples in all the categories of newborns in relation to their maturity and birth weight.

Table-20 depicts the comparison of cord blood passive measles HAI antibody titres (GMT) in relation to sex; maturity and birth weight and maturity of newborns.

Antibody titres (GMT) did not significantly differ in males as compared to females.

Similarly, the maturity and birth weight of newborns did not significantly influence antibody titres.

Tables-18, 19, and 20 thus demonstrated that-

- There is no active transplacental transfer of measles HAI antibody.

TABLE-19

COMPARISON BETWEEN MATERNAL (M) AND CORD BLOOD (F) MEASLES HAI ANTIBODY TITRES (GMT) IN RELATION TO THE MATURITY[a] AND BIRTH WEIGHT OF NEWBORNS

Sub-group	Variable	n	GMT Mean ± S.E.	't' test value
FT	GMT - M	169	3.16 ± 0.11	0.50 - N.S.
	GMT - F	169	3.11 ± 0.11	
FTAGA	GMT - M	151	3.15 ± 0.12	0.57 - N.S.
	GMT - F	151	3.09 ± 0.12	
FTSGA	GMT - M	18	3.28 ± 0.39	0.37 - N.S.
	GMT - F	18	3.33 ± 0.34	
PT	GMT - M	18	4.17 ± 0.41	1.74 - N.S.
	GMT - F	18	3.39 ± 0.42	
PTAGA	GMT - M	11	4.09 ± 0.51	0.97 - N.S.
	GMT - F	11	3.55 ± 0.53	
PTSGA	GMT - M	7	4.29 ± 0.71	1.49 - N.S.
	GMT - F	7	3.14 ± 0.74	

(a) = As per Dubowitz's classification (79)
FT = Full term
FTAGA = Full term appropriate for gestational age
FTSGA = Full term small for gestational age
PT = Preterm
PTAGA = Preterm appropriate for gestational age
PTSGA = Preterm small for gestational age
N.S. = Not significant

TABLE-20

COMPARISON OF CORD BLOOD PASSIVE MEASLES HAI ANTIBODY TITRES (GMT) IN RELATION TO SEX, MATURITY [(a)] AND BIRTH WEIGHT AND MATURITY [(a)] OF NEWBORNS

Variable	n	GMT Mean ± S.E.	't' test value
Male	95	3.26 ± 0.14	1.18 - N.S.
Female	92	3.01 ± 0.16	
FT	169	3.11 ± 0.11	0.76 - N.S.
PT	18	3.39 ± 0.42	
FTGA	151	3.09 ± 0.12	0.70 - N.S.
FTSGA	18	3.33 ± 0.34	
PTAGA	11	3.55 ± 0.53	0.46 - N.S.
PTSGA	7	3.14 ± 0.74	

(a) = As per Dubowitz's classification (79)
FT = Full term
PT = Preterm
FTAGA = Full term appropriate for gestational age
FTSGA = Full term small for gestational age
PTAGA = Preterm appropriate for gestational age
PTSGA = Preterm small for gestational age
N.S. = Not significant

- Intrauterine growth retardation and/or prematurity have no effect on cord blood measles HAI antibody titres.
- The intrauterine transplacental transfer of measles HAI antibody probably occurs before 28 weeks of gestation.

Measles HAI antibody has been reported to be detectable by as early as 13-15 weeks of gestation (157).

In similar studies from Vadodara, Dholakia (72) and Vasani (334) reported passive transplacental transfer of measles HAI antibody. Also, no difference was observed when maturity and intrauterine growth retardation were taken into account.

To summarise, the results of the Maternal vs. Cord Blood Study highlighted the following points-

1. A highly significant correlation was observed between maternal and cord blood measles HAI antibody titres (Fig.9).
2. The maturity, birth weight and sex of newborns did not influence the levels of measles HAI antibody.
3. The transplacental transfer of measles HAI antibody appeared to be passive.
4. The transplacental transfer of measles HAI antibody seemed to be completed before 28 weeks of gestation.

B. Waning of Passive Measles HAI Antibody Study

A total of 623 cases were included for studying the waning of passive measles HAI antibody titre in children (0-72 months) who had no history of measles or measles vaccination.

Table-21 gives the percent distribution of children (0-72 months) in relation to their age and sex. Out of the total sample of 623, 57.78% were males and 42.22% were females.

Effect of age on waning of passive measles HAI antibody

One of the three major factors to be considered while determining

FIGURE-9

CORRELATION BETWEEN MATERNAL(M) AND CORD(F) BLOOD MEASLES HAI ANTIBODY TITRES(GMT)

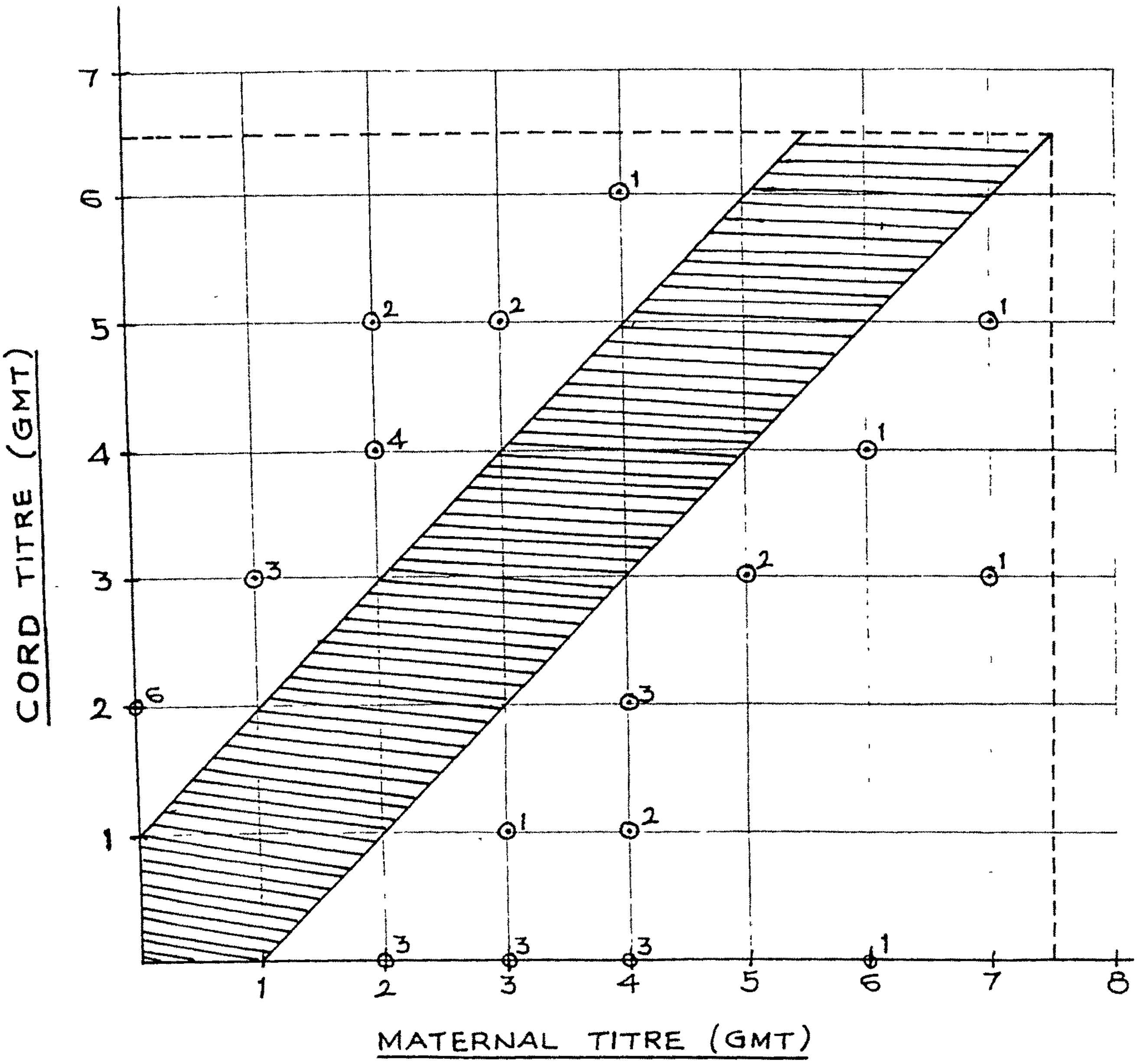


TABLE-21

PERCENT DISTRIBUTION OF CHILDREN (0-72 MONTHS) IN

RELATION TO THEIR AGE AND SEX

Age group (months)	Male	Female	Total
0	7.38 (46)	6.10 (38)	13.48 (84)
3-5	3.85 (24)	2.09 (13)	5.94 (37)
6-8	7.71 (48)	7.54 (47)	15.25 (95)
9-11	16.53 (103)	9.95 (62)	26.48 (165)
12-14	6.74 (42)	5.78 (36)	12.52 (78)
15-17	0.64 (4)	1.77 (11)	2.41 (15)
18-20	6.10 (38)	2.25 (14)	8.35 (52)
21-23	1.61 (10)	0.80 (5)	2.41 (15)
24-72	7.22 (45)	5.94 (37)	13.16 (82)
Total	57.78 (360)	42.22 (263)	100.00 (623)

Total percent distribution
Figures in parentheses indicate the number of subjects.

the earliest possible age for measles vaccination is the time of waning of passive measles antibody (349).

Table-22 shows the percent distribution of passive measles HAI antibody titres in relation to age in children (0-72 months).

At birth, 5.95% children were seronegative. However, there was a remarkable increase in seronegativity in children upto 8 months of age. In the age group 3-5 months and 6-8 months, 40.54% and 78.95% of children respectively had lost maternal measles HAI antibody.

The results of the present study correlate well with other studies. Mehta et al (219) have observed seronegativity of 30%, 25% and 75% at birth, 3 months and 6 months respectively. John (140) has shown that 17% of children between 0-3 months and 75% of children between 3-6 months were seronegative for measles HAI antibody. A WHO-sponsored study in Kenya has reported 100% seropositivity at birth and 87.1% and 26.8% seropositivity at 3 months and 6 months respectively (349). Agrawal (5) has reported that 90% of infants lose passive measles HAI antibody by the age of 7 months. Man Mohan et al (199) too have demonstrated that by the age of 8 months, the majority of infants become seronegative.

Various other authors have also reported a similar significant fall in the passive measles HAI antibody titre by the age of 6-8 months (68,197,305,310,312,323).

On studying the association between the presence of passive measles HAI antibody and the age of children (Table-23), a statistically significant ($P \leq 0.001$) inverse relationship was observed from birth to the age of 8 months. Thereafter, this inverse relationship was not maintained, showing a gradual increase in seropositivity with the increase in age. However, there were intermittent falls in the 15-17 months and 21-23 months age groups. These differences in seropositivity in successive age groups were statistically non-significant.

Similar association between levels of passive measles HAI antibody (GMT) and age of children was observed (Table-24).

TABLE-22

PERCENT DISTRIBUTION OF PASSIVE MEASLES HAI ANTIBODY

TITRES IN RELATION TO AGE IN CHILDREN (0-72 MONTHS)

Age group (months)	Titre						
	1:2	1:2	1:4	1:8	1:16	1:32	1:64
0 (84)	5.95 (5)	8.33 (7)	20.24 (17)	17.86 (15)	27.38 (23)	19.05 (16)	1.19 (1)
3-5 (37)	40.54 (15)	32.43 (12)	16.21 (6)	5.41 (2)	5.41 (2)	-	-
6-8 (95)	78.95 (75)	12.63 (12)	3.16 (3)	3.16 (3)	1.05 (1)	1.05 (1)	-
9-11 (165)	76.97 (127)	9.09 (15)	7.27 (12)	4.24 (7)	1.82 (3)	0.61 (1)	-
12-14 (78)	67.95 (53)	10.26 (8)	15.39 (12)	1.28 (1)	2.56 (2)	-	2.56 (2)
15-17 (15)	80.00 (12)	-	6.67 (1)	-	-	13.33 (2)	-
18-20 (52)	59.61 (31)	9.61 (5)	23.08 (12)	5.78 (3)	1.92 (1)	-	-
21-23 (15)	66.66 (10)	20.00 (3)	6.67 (1)	-	6.67 (1)	-	-
24-72 (82)	57.32 (47)	8.54 (7)	20.72 (17)	7.32 (6)	4.88 (4)	1.22 (1)	-

Row percent distribution
Figures in parentheses indicate number of subjects.

TABLE-23

PERCENT DISTRIBUTION OF AND ASSOCIATION BETWEEN THE PRESENCE OF PASSIVE MEASLES HAI ANTIBODY AND AGE IN CHILDREN (0-72 MONTHS)

Group	Age group (months)	Percent distribution		Chi-square value
		Seropositive	Seronegative	
a	0 (84)	94.05 (79)	5.95 (5)	
b	3-5 (37)	59.46 (22)	40.54 (15)	a vs. b 19.84 ***
c	6-8 (95)	21.05 (20)	78.95 (75)	b vs. c 18.11 ***
d	9-11 (165)	23.03 (38)	76.97 (127)	c vs. d 0.14 - N.S.
e	11-14 (78)	32.05 (25)	67.95 (53)	d vs. e 2.24 - N.S.
f	15-17 (15)	20.00 (3)	80.00 (12)	e vs. f(a) 0.39 - N.S.
g	18-21 (52)	40.39 (21)	59.81 (31)	f vs. g(a) 1.31 - N.S.
h	21-23 (15)	33.33 (5)	66.67 (10)	g vs. h(a) 0.37 - N.S.
i	24-72 (82)	42.68 (35)	57.32 (47)	h vs. i(a) 0.15 - N.S.
Total	0-72 (623)	39.81 (248)	60.19 (375)	

Row percent distribution
Figures in parentheses indicate number of subjects.
*** = Significant at $P \leqslant 0.001$
N.S. = Not significant
(a) = After Yates' correction

TABLE-24

ASSOCIATION BETWEEN PASSIVE MEASLES HAI ANTIBODY TITRES (GMT)

AND AGE IN CHILDREN (0-72 MONTHS)

Group	Age group (months)	n	GMT Mean ± S.E.	't' test value
a	0	84	3.14 ± 0.16	a vs. b 7.69***
b	3-5	37	1.03 ± 0.19	b vs. c 3.41***
c	6-8	95	0.38 ± 0.09	c vs. d 0.70 - N.S.
d	9-11	165	0.47 ± 0.08	d vs. e 1.43 - N.S.
e	12-14	78	0.71 ± 0.15	e vs. f 0.24 - N.S.
f	15-17	15	0.80 ± 0.46	f vs. g 0.02 - N.S.
g	18-20	52	0.81 ± 0.15	g vs. h 0.64 - N.S.
h	21-23	15	0.60 ± 0.29	h vs. i 1.04 - N.S.
i	24-72	82	0.98 ± 0.15	

*** = Significant at $P \leq 0.001$
N.S. = Not significant

On comparing the GMT levels, a highly significant ($P \leq 0.001$) fall was observed between age groups 0 and 3-5 months (3.14 vs. 1.03) and between age groups 3-5 months and 6-8 months (1.03 vs. 0.38). Thereafter, there was a gradual consistent increase in mean GMT levels from 0.38 in the 6-8 months age groups to 0.98 in the 24-72 months age group, the differences in successive age groups being statistically non-significant.

In the present study, measles seropositivity rate after 8 months of age showed a rising trend but with intermittent falls. It was observed that 32.05%, 40.39% and 42.68% were seropositive in the age groups 12-14 months, 18-20 months and 24-72 months respectively. An intermittent fall was observed with 20.00% and 33.34% seropositivity in the age groups 15-17 months and 21-23 months respectively. Similarly, levels of passive measles HAI antibody (GMT), showed a rising trend but with an intermittent fall, after 8 months of age. This increase in seropositivity and levels of antibody with the increasing age, in the absence of clinical manifestations of measles as well as measles vaccination, suggests the possibility of subclinical infection in these children.

Till recently, subclinical measles infection was considered a rarity (13,242). However, recent studies by several investigators (72,77,83, 140,141,162,180,197,219) have substantiated the concept of subclinical measles infection by demonstrating a rise in the number of seropositive children beyond 9 months of age which is in accordance with the results of the present study. Stokes et al (311) have postulated that this phenomenon may be related to exposure to infection while the infant still has residual passive antibody which is sufficient to protect from disease but not enough to prevent infection.

In a study by John et al (141), serological evidence of measles infection was observed in over 30% of the children between 1 and 5 years of age, in whom a history of measles was denied. In a report by Mehta and co-workers (219), it was observed that 38% of children in the age group 1 to 5 years had demonstrable measles virus neutralising antibody.

Dholakia (72) has reported 25% of children in the same age group to be seropositive.

In a recent study from Delhi, Dutta et al (83) have reported passive HAI antibody seropositivity of 38.5%, 17.6%, 14.3% and 52.5% at the age of 6-8 months, 9-11 months, 12-18 months and more than 18 months respectively. Dongre et al (180) have reported a similar increase in seropositivity after the age of 7 months.

Khare et al (162) reported seropositivity of 44.9% in children aged 1-8 years who gave no history of measles or immunisation. In the present study also, 36.77% of the children in the 1-6 years age group, who gave no history of measles or vaccination were seropositive.

On comparing the values of the quantitative parameter (GMT) of the present study with other studies (5,67,72,305,349), a similar inverse relationship between the levels of measles antibody and age (birth to 8 months) was observed.

In a study conducted by WHO in Kenya (349), a rapid fall in passive measles immunity from birth to 7½ months followed by a plateau has been demonstrated. Man Mohan et al (199) also have reported a rapid fall in antibody titre from birth to the age of 8 months after which it remained almost static. Similar findings have been reported by other authors (67,305).

However, authors from the developed countries (7,171,356) have reported that the majority of infants become seronegative by 11-12 months of age. The possible explanation offered for this observation is that infants in the developing countries lose their passively acquired measles antibodies at a faster rate than their counterparts in the developed countries (109) and the children in the developed countries are not exposed to recurrent natural infection.

To conclude, with relevance to passive measles HAI antibody, there was a rapid decline both in the number of seropositive children as well as their antibody levels (GMT) from birth to 8 months.

Effect of nutritional status on waning of passive measles HAI antibody

Table-25 describes the percent distribution of the presence of passive measles HAI antibody in relation to PEM grade in children (6-72 months). The children upto the age of 6 months were excluded as they fall outside the purview of the IAP Classification (249).

Though an increasing trend in seropositivity was observed with the increase in PEM grade, statistically no significant difference was obtained when comparisons were made within various groups.

A greater number of children in normal nutritional grade could possibly be explained on the basis of purposive selection of subjects for the study wherein those with a past history of measles disease or vaccination could not be included.

Similarly, no significant association was observed between passive measles HAI antibody levels (GMT) and PEM grades in children (6-72 months) when comparison was made within various groups (Table-26).

Similar results have been reported by Agrawal (5), Man Mohan et al (199) and a WHO study conducted in Kenya (349).

However, Halsey et al (109) have reported a rapid decline in passive measles antibody in malnourished children as compared to well nourished children. The investigators postulated that these malnourished children from the developing countries might be metabolising the maternal antibodies in order to selectively preserve their own protein stores.

To summarise, nutritional status of children was found to have no effect both on the number of seropositive children as well as on their passive measles HAI antibody levels (GMT).

Effect of sex on waning of passive measles HAI antibody

Table-27 depicts the association between the presence of passive measles HAI antibody and sex of children (6-72 months). No difference was observed in frequency distribution of passive measles HAI antibody between male and female children.

TABLE-25

PERCENT DISTRIBUTION OF AND ASSOCIATION BETWEEN THE PRESENCE OF PASSIVE MEASLES HAI ANTIBODY AND NUTRITIONAL STATUS [(a)] IN CHILDREN (6-72 MONTHS)

Group	PEM[(a)] grade	Distribution *		Chi-square value
		Seropositive	Seronegative	
a	0 (303)	26.73 (81)	73.27 (222)	a vs. b 0.46 - N.S.
b	I (113)	30.09 (34)	69.91 (79)	a vs. c 2.72 - N.S.
c	II (65)	36.92 (24)	63.08 (41)	a vs. d[(b)] 1.15 - N.S.; b vs. c 0.89 - N.S.
d	III+IV (21)	38.10 (8)	61.90 (13)	b vs. d [(b)] 0.50 - N.S.
	Total (502)	29.28 (147)	70.72 (355)	c vs d [(b)] 0.0 - N.S.

* Row percent distribution
(a) = As per IAP Classification (Annexure : 2)
Figures in parentheses indicate number of subjects.
N.S. = Not significant
(b) = After Yates' correction

TABLE-26

ASSOCIATION BETWEEN PASSIVE MEASLES HAI ANTIBODY TITRES (GMT) AND NUTRITIONAL STATUS [a] IN CHILDREN (6-72 MONTHS)

Group	PEM[a] grade	n	GMT Mean ± S.E.	Oneway anova of GMT by PEM [a]
a	0	303	0.61 ± 0.07	
b	I	113	0.60 ± 0.11	F ratio 0.97
c	II	65	0.66 ± 0.12	F probability 0.41 - N.S.
d	III+IV	21	0.67 ± 0.22	

(a) = As per IAP Classifiction (Annexure : 2)
N.S. = Not significant

TABLE-27

PERCENT DISTRIBUTION OF AND ASSOCIATION BETWEEN THE PRESENCE OF PASSIVE MEASLES HAI ANTIBODY AND SEX IN CHILDREN (0-72 MONTHS)

Sex	Seropositive	Seronegative	Chi-square value
Male	40.83 (147)	59.17 (213)	
			0.37 - N.S.
Female	38.40 (101)	61.60 (162)	
Total (623)	39.80 (248)	60.20 (375)	

Row percent distribution
Figures in parentheses indicate number of subjects.
N.S. = Not significant

TABLE-28

ASSOCIATION BETWEEN PASSIVE MEASLES HAI ANTIBODY TITRES (GMT) AND SEX IN CHILDREN (0-72 MONTHS)

Sex	n	GMT Mean ± S.E.	't' test value
Male	360	0.98 ± 0.08	0.07 - N.S.
Female	263	0.99 ± 0.09	

N.S. = Not significant

FIGURE-10

FALL IN PASSIVE MEASLES HAI ANTIBODY TITRES (GMT)
IN VARIOUS AGE GROUPS (0-72 MONTHS)

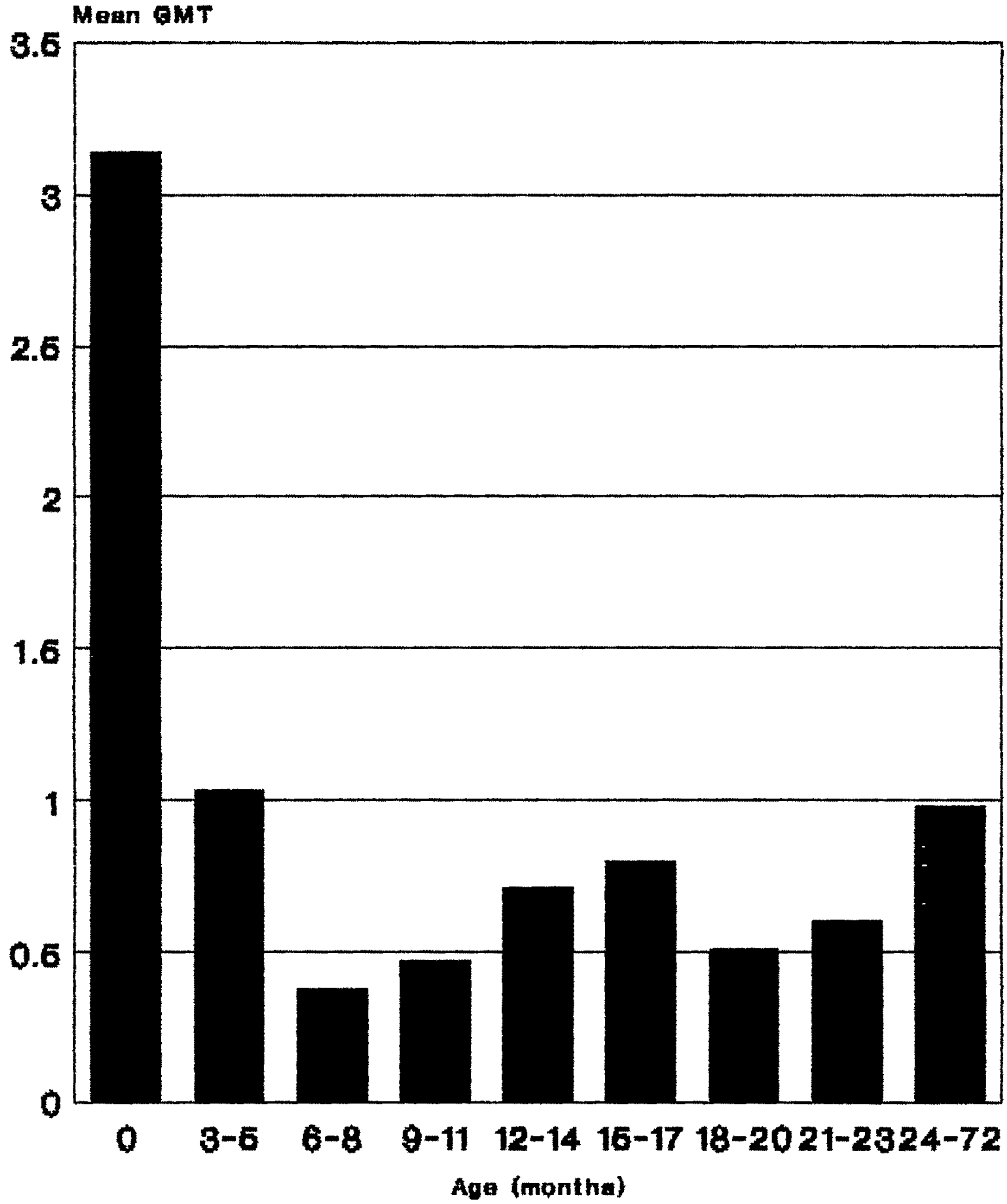


FIGURE-11

FALL IN PASSIVE MEASLES HAI ANTIBODY SEROPOSITIVITY
IN VARIOUS AGE GROUPS (0-72 MONTHS)

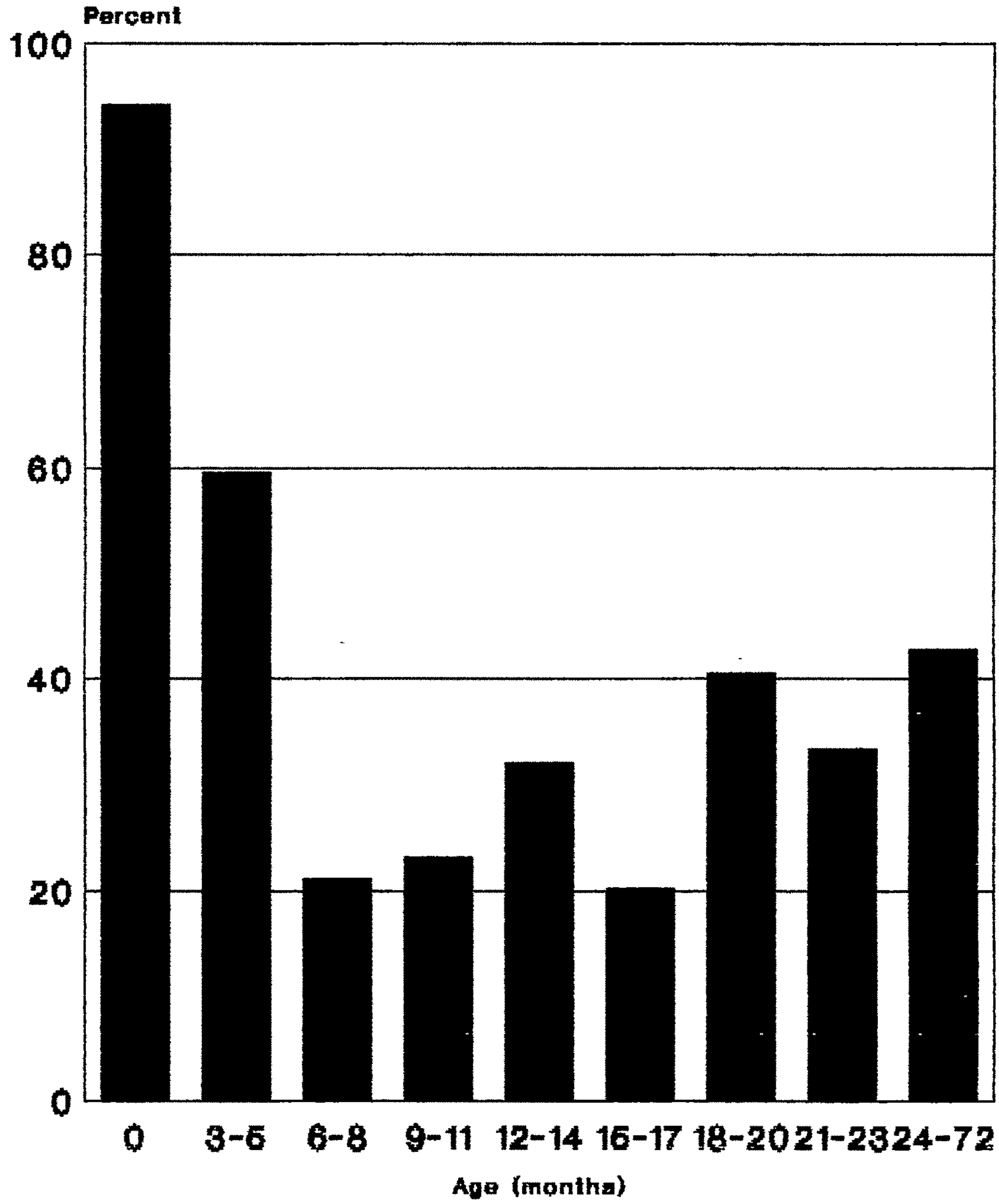


TABLE-29

PERCENT DISTRIBUTION OF CHILDREN (6-72 MONTHS) IN

RELATION TO THEIR AGE AND SEX

Age group (months)	Male	Female	Total
6-8	5.20 (17)	2.14 (7)	7.34 (24)
9-11	20.18 (66)	13.46 (44)	33.64 (110)
12-14	9.18 (30)	8.87 (29)	18.05 (59)
15-17	0.92 (3)	2.45 (8)	3.37 (11)
18-20	11.31 (37)	3.67 (12)	14.98 (49)
21-23	2.14 (7)	0.61 (2)	2.75 (9)
24-72	11.31 (37)	8.56 (28)	19.87 (65)
Total	60.24 (197)	39.76 (130)	100.00 (327)

Total percent distribution
Figures in parentheses indicate number of subjects.

TABLE-30

PERCENT DISTRIBUTION OF PREVACCINATION MEASLES HAI ANTIBODY TITRES

ACCORDING TO AGE AT VACCINATION IN CHILDREN (6-72 MONTHS)

Titre	Age at vaccination (months)							Total
	6-8	9-11	12-14	15-17	18-20	21-23	24-72	
<1:2	75.0 (18)	80.9 (89)	64.4 (38)	72.7 (8)	61.2 (30)	66.7 (6)	52.3 (34)	68.20 (223)
1:2	-	11.8 (13)	11.9 (7)	-	8.2 (4)	22.2 (2)	10.8 (7)	10.09 (33)
1:4	16.67 (4)	5.5 (6)	18.6 (11)	9.1 (1)	24.5 (12)	11.1 (1)	23.1 (15)	15.29 (50)
1.8	8.33 (2)	1.8 (2)	1.7 (1)	-	6.1 (3)	-	9.2 (6)	4.28 (14)
1:16	-	-	3.4 (2)	-	-	-	4.6 (3)	1.52 (5)
1:32	-	-	-	9.1 (1)	-	-	-	0.31 (1)
1:64	-	-	-	9.1 (1)	-	-	-	0.31 (1)
Total 100%	(24)	(110)	(59)	(11)	(49)	(9)	(65)	(327)

Column percent distribution
Figures in parentheses indicate number of subjects.

TABLE-31

PERCENT DISTRIBUTION OF POSTVACCINATION MEASLES HAI ANTIBODY TITRES ACCORDING TO AGE AT VACCINATION IN CHILDREN (6-72 MONTHS)

Titre	Age at vaccination (months)							Total
	6-8	9-11	12-14	15-17	18-20	21-23	24-72	
<1·2	75.0 (18)	11.8 (13)	5.1 (3)	9.1 (1)	8.2 (4)	-	4.6 (3)	12.84 (42)
1:2	-	2.7 (3)	1.7 (1)	-	-	-	-	1.23 (4)
1:4	8.3 (2)	6.4 (7)	6.8 (4)	-	8.2 (4)	-	4.6 (3)	6.12 (20)
1:8	12.5 (3)	15.5 (17)	25.4 (15)	27.3 (31)	20.4 (10)	55.6 (5)	26.2 (17)	21.41 (70)
1:16	-	33.6 (37)	27.1 (16)	27.3 (3)	26.5 (13)	20.2 (21)	24.6 (16)	26.61 (87)
1:32	-	23.6 (26)	16.9 (10)	18.1 (2)	28.6 (14)	11.1 (1)	21.5 (14)	20.48 (67)
1:64	4.2 (1)	6.4 (7)	10.2 (6)	9.1 (1)	6.1 (3)	11.1 (1)	12.3 (8)	8.26 (27)
1:128	-	-	-	9.1 (1)	-	-	-	0.30 (1)
1:256	-	-	5.1 (3)	-	2.0 (1)	-	6.2 (4)	2.45 (8)
1:512	-	-	1.7 (1)	-	-	-	-	0.30 (1)
Total 100%	(24)	(110)	(59)	(11)	(49)	(09)	(65)	(327)

Column percent distribution
Figrues in parentheses indicate number of subjects.

The highest prevaccination titre in children $<$12 months of age was 1:8, while the same was 1:64 in children $\geq$12 months of age. The postvaccination titre (Table-31) in most of the children (95.89%) was $\leq$1:64; only one child had postvaccination titre of 1:512.

Table-32 and Table-33 demonstrate the percent distribution of children (6-72 months) who seroconverted in relation to pre- and postvaccination measles HAI antibody titre respectively and age at vaccination.

A minimum four-fold rise in prevaccination titre was considered a successful seroconversion.

Table-34 depicts the percent distribution of children (6-72 months) who seroconverted in relation to pre- and postvaccination measles HAI antibody titres.

Seroconversion rate following measles vaccination given earlier than 12 months of age is also an important factor to be considered while determining the optimum age for measles immunisation (349).

Based on the percent distribution data shown in Table-30 to Table-34, the effect of age at vaccination and prevaccination titre on seroconversion rates was analysed The results of this analysis are presented in Table-35 and Table-36.

Effect of age at vaccination on seroconversion

Table-35 demonstrates the association between seroconversion and age at the time of vaccination in children (6-72 months).

In the 6-8 months age group, only 25% of children seroconverted while in the 9-11 months age group, 80.91% of children seroconverted. This difference in seroconversion rates was highly significant (P $\leq$0.001).

Though seroconversion rates from 9-11 months to 24-72 months age groups varied from 63.66% to 88.88%, when comparisions were made between successive age groups, no significant difference was observed.

TABLE-32

PERCENT DISTRIBUTION ACCORDING TO PREVACCINATION MEASLES HAI ANTIBODY TITRES AND AGE AT VACCINATION IN CHILDREN (6-72 MONTHS) WHO SEROCONVERTED (FOUR-FOLD RISE)

Titre	Age at vaccination (months)						
	6-8	9-11	12-14	15-17	18-20	21-23	24-72
< 1:2	25.00 (6/24)	83.15 (74/89)	89.47 (34/38)	87.50 (7/8)	86.66 (26/30)	100.00 (6/6)	97.06 (33/34)
1:2	-	84.61 (11/13)	85.71 (6/7)	-	100.00 (4/4)	100.00 (2/2)	85.71 (6/7)
1:4	-	66.66 (4/6)	63.64 (7/11)	0.00 (0/1)	66.66 (8/12)	0.00 (0/1)	40.00 (6/15)
1:8	-	0.00 (0/2)	0.00 (0/1)	-	0.00 (0/3)	-	50.00 (3/6)
≥ 1:16	-	-	0.00 (0/2)	0.00 (0/2)	-	-	0.00 (0/3)

Subgroup percent distribution
Figures in parentheses indicate number of subjects who seroconverted (numerator) and number of total subjects in the subgroup (denominator); percentages shown are for the same subgroup.

TABLE-33

PERCENT DISTRIBUTION ACCORDING TO AGE AT VACCINATION AND POSTVACCINATION MEASLES HAI ANTIBODY TITRES IN CHILDREN (6-72 MONTHS) WHO SEROCONVERTED (FOUR-FOLD RISE)

Titre	Age at vaccination (months)						
	6-8	9-11	12-14	15-17	18-20	21-23	24-72
1:4	20.00 (2)	50.00 (5)	10.00 (1)	-	20.00 (2)	-	-
1:8	5.77 (3)	28.85 (15)	23.08 (12)	1.92 (1)	15.38 (8)	7.69 (4)	17.31 (9)
1:16	-	45.57 (36)	18.99 (15)	3.80 (3)	12.66 (10)	2.53 (2)	16.45 (13)
1:32	-	39.39 (26)	13.64 (9)	3.03 (2)	21.21 (14)	1.52 (1)	21.21 (14)
1:64	3.70 (1)	25.93 (7)	18.52 (5)	7.41 (2)	11.11 (3)	3.70 (1)	29.63 (8)
1:256	-	-	37.50 (3)	-	12.50 (1)	-	50.00 (4)
1:512	-	-	100.00 (1)	-	-	-	-

Row percent distribution
Figures in parentheses indicate number of subjects.

TABLE-34

PERCENT DISTRIBUTION ACCORDING TO PRE-AND POSTVACCINATION MEASLES HAI

ANTIBODY TITRES IN CHILDREN (6-72 MONTHS)

WHO SEROCONVERTED (FOUR-FOLD RISE)

Pre-vaccination titre	Postvaccination titre 1:4	1:8	1:16	1:32	1:64	1:128	1:256	1:512	Row total 100%
<1:2	5.38 (10)	23.12 (43)	33.33 (62)	25.27 (47)	9.14 (17)	-	3.76 (7)	-	(186)
1:2	-	30.00 (9)	23.33 (7)	26.67 (8)	13.33 (4)	-	-	3.33 (1)	(30)
1:4	-	-	40.00 (10)	40.00 (10)	16.00 (4)	-	4.00 (1)	-	(25)
1·8	-	-	-	33.33 (1)	66.67 (2)	-	-	-	(3)

Row percent distribution
Figures in parentheses indicate number of subjects.

TABLE-35

ASSOCIATION BETWEEN SEROCONVERSION (FOUR-FOLD RISE) AND AGE AT VACCINATION IN CHILDREN (6-72 MONTHS)

Group	Age group (months)	Sero-P	Sero-N	Chi-square value
a	6-8	25.00 (6)	75.00 (18)	
b	9-11	80.91 (89)	19.09 (21)	a vs. b[a] 27.20***
c	12-14	79.66 (47)	20.34 (12)	b vs. c 0.07 - N.S.
d	15-17	63.66 (7)	36.34 (4)	c vs. d[a] 1.17 - N.S.
e	18-20	77.55 (38)	22.45 (11)	d vs. e[a] 0.84 - N.S.
f	21-23	88.88 (8)	11.12 (1)	e vs. f[a] 1.07 - N.S.
g	24-72	73.85 (48)	26.15 (17)	f vs. g[a] 1.46 - N.S.
h	9-72	78.22 (237)	21.78 (66)	a vs. h[a] 31.69***

Row percent distribution
Sero-P = Successful seroconversion (four-fold rise)
Sero-N = No seroconversion
Figures in parentheses indicate number of subjects.
(a) = After Yates' correction
*** = Significant at $P \leq 0.001$
N.S. = Not significant

Overall, 78.22% children in the age group of 9-72 months seroconverted, as compared to only 25% children in the age group of 6-8 months. This difference in seroconversion rates was found to be statistically highly significant ($P \leq 0.001$).

Variable observations have been reported regarding seroconversion rates during infancy. One major reason for this variability is not considering a minimum four-fold rise in prevaccination titre levels as a successful seroconversion, as was done in the present study.

As reviewed by Feachem and Koblinsky (94), age-specific seroconversion rates following measles vaccination ranged from 23% to 95% in age groups 6 months to 12 months.

Similarly, Kaur et al (157) have considered a four-fold rise as seroconversion and reported 33.3% and 80% seroconversion rates at 6 months and 8 months of age respectively.

Krugman (179) has reported 86% and 97% seroconversion rates respectively at 9-11 months and $\geq$12 months of age.

Dholakia (72) has reported a four-fold or more rise from prevaccination titre in 78.8% and 77.2% children in age groups of 9-12 months and 13-60 months respectively.

Dutta et al (81) have reported 78.57% seroconversion (four-fold rise) in 9-11 months age group.

Bhaskaram et al (22) reported higher seroconversion failure rate in children under the age of 15 months as compared to those above the age of 15 months (protective titre >1:8).

Reynolds et al (269) have observed seroconversion rate of 79% for children below one year of age and 100% for children above one year of age.

Other studies from USA (7,64,176,188,356) and Canada (264) have consistently reported lower rates of seroconversion in children vaccinated under the age of one year.

Contrary to the findings of the present study, Agrawal (5), Job et al (138) and Meyer et al (222) have reported high seroconversion rates at an early age of vaccination.

Agrawal (5) has reported a 81.5% seroconversion (four-fold rise) rate at the age of 6 months.

Similarly, Job et al (138) have reported 87% seroconversion at 6-8 months of age. However, these investigators considered children with titre less than 1:4 as seronegative and those who acquire antibody after measles vaccination as seroconverted.

Meyer et al (222) also have reported 90% seroconversion at 7 months of age.

More indepth studies are thus required to study the seroconversion rates in 6-9 months age group using a standard protocol.

Effect of prevaccination titre on seroconversion

Table-36 describes the association between prevaccination titre and seroconversion in children aged 6-72 months.

An inverse relationship was observed between prevaccination titre and seroconversion rate. A statistically significant difference (p 0.01) in seroconversion was observed when comparison was made between prevaccination titre $\leq$ 1:2 and 1:4. With a prevaccination titre $\leq$ 1:2, the seroconversion rate was maximum (82.06%). None with prevaccination titre $\geq$1:16 demonstrated a four-fold rise (seroconversion).

The results of the present study corroborated well with other reported studies. Different studies have reported that pre-existing passive measles HAI antibody does hamper the take of measles vaccine. In a WHO study from Kenya (349) where 5-12 month old children were studied, with a prevaccination negative titre, the seroconversion rate was 60-100%, while with a prevaccination titre of 1:3, the seroconversion rate fell to 17.65% and with a titre of 1:6, only 7.65% seroconverted. None of those with prevaccination titre of 1:12 showed seroconversion.

TABLE-36

ASSOCIATION BETWEEN SEROCONVERSION (FOUR-FOLD RISE) AND PREVACCINATION TITRE IN CHILDREN (6-72 MONTHS)

Group	Titre	Sero-P	Sero-N	Chi-square value
a (229)	< 1·2	81.2 (186)	18.8 (43)	
b (33)	1 2	87.9 (29)	12.1 (4)	a vs. b[a] 0.25 - N.S.
c (46)	1.4	54.3 (25)	45.7 (21)	b vs. c[a] 10.12**
d (12)	1.8	25.0 (3)	75.0 (9)	c vs. d[a] 3.42 - N.S.
e (7)	≥1.16	0.0 (0)	100.0 (7)	a+b vs. c+d+e 41.45***

Row percent distribution
Figures in parentheses indicate number of subjects.
(a) = After Yates' correction
N.S. = Not significant
** = Significant at $P \leq 0.01$
*** = Significant at $P \leq 0.001$

In a study by Agrawal (5), seroconversion rates (four-fold rise) of 91.6% and 90.5% were reported with prevaccination titres of 0 and 1:2 respectively, which dropped to 50% when the prevaccination titre was $\ngeq$ 1.16.

Dholakia (72) has reported 88% and 82.8% seroconversion rates (four-fold rise) when prevaccination titres were 0 and 1:2 respectively. They fell to 51.1% and 27.3% when prevaccination titres were 1:4 and 1:8 respectively. None seroconverted when the prevaccination titre was $\ngeq$ 1:16.

Dutta et al (83) have also reported a seroconversion rate (four-fold rise) of 85.7% when prevaccination titre was ∠1:8, 33.3% when prevaccination titre was 1:8 and none when prevaccination titre was 1:16 in 9-11 months old children.

Similarly, Kaur et al (157) have reported an inverse relationship between prevaccination titre and seroconversion rate (four-fold rise). Seroconversion rates of 76.2% and 40% were reported with prevaccination titres of $<$ 1:4 and $\geq$ 1:4 respectively, and no seroconversion at titres 1:32 or more.

Similar findigs have been reported by Bhatnagar et al (24), Ghosh et al (101) and Katiyar et al (151).

To conclude, when seroconversion rates were analysed considering both the age at vaccination and the prevaccination titre, it was observed that the seroconversion was maximum after the age of 8 months and with a prevaccination titre less than 1:4.

Effect of nutritional status on seroconversion

Table-37 describes the association between seroconversion and nutritional status in children (6-72 months).

No significant difference was observed on analysing the seroconversion rates within the various subgroups.

These findings are corroborated by studies of Agrawal (5), Bhatanagar (24), Dholakia (72), Ifekwunigwe (132), Job et al (138), Kantharia (150), Katiyar et al (151), Marshal et al (203) and MC Murray et al (211).

TABLE-37

ASSOCIATION BETWEEN SEROCONVERSION (FOUR-FOLD RISE) AND NUTRITIONAL STATUS[a] IN CHILDREN (6-72 MONTHS)

PEM[a] grade	Sero-P	Sero-N	Chi-square value
0	70.62 (125)	29.38 (52)	
I	82.76 (72)	17.24 (15)	
II	75.56 (34)	24.44 (11)	5.10 - N.S.
III+IV	66.69 (12)	33.33 (6)	
Total (327)	74.31 (243)	25.69 (84)	

Row percent distribution
(a) = As per IAP Classification (Annexure : 2)
Sero-P = Successful seroconversion (four-fold rise)
Sero-N = No seroconversion
Figures in parentheses indicate number of subjects.

However, in a study by Hafez et al (108), malnourished children were reported to have failed to seroconvert following measles vaccination.

Chandra et al (52) have reported that though malnourished children develop normal levels of measles neutrulising antibody, they fail to develop secretory IgA antibody.

Wesley et al (339) have reported that although the overall response rate was equal to that of well nourished children, malnourished children developed serum antibody slower than normal children.

In contrast, a study conducted in Latin America (223) has demonstrated higher seroconversion rates in malnourished children attributing this to faster and earlier loss of passive protection.

Though malnutrition has been associated with alteration in the immune response, the administration of measles vaccine to malnourished children appears to be safe and effective (109).

Considering the high morbidity and mortality due to measles in the malnourished children, far from being a contra-indication malnutrition is an urgent indication for measles immunisation.

Effect of sex on seroconversion

Table-38 depicts the association between seroconversion rate and sex of children.

No statistically significant difference was observed in seroconversion rates between male and female children.

Similar findings have been reported by Agrawal (5) Bhatnagar (24) and Dholakia (72).

Effect of age at vaccination on postvaccination rise in measles HAI antibody titres (GMT)

Table-39 gives the percent distribution of seroconverted children, according to postvaccination rise in GMT and age at vaccination.

TABLE-38

ASSOCIATION BETWEEN SEROCONVERSION (FOUR-FOLD RISE)

AND SEX IN CHILDREN (6-72 MONTHS)

Sex	Sero-P	Sero-N	Chi-square value
Male	59.26 (144)	40.74 (99)	
			0.38 - N.S.
Female	63.10 (53)	36.90 (31)	
Total (327)	60.25 (197)	39.75 (130)	

Row percent distribution
Sero-P = Successful seroconversion (four-fold rise)
Sero-N = No seroconversion
Figures in parentheses indicate number of subjects.
N.S. = Not significant

TABLE-39

PERCENT DISTRIBUTION ACCORDING TO POSTVACCINATION RISE IN MEASLES HAI ANTIBODY TITRES (GMT) AND AGE AT VACCINATION IN CHILDREN (6-72 MONTHS) WHO SEROCONVERTED (FOUR-FOLD RISE)

Age at vaccination (months)	Rise in postvaccination (GMT)					
	2	3	4	5	6	8
6-8	33.33 (2)	50.00 (3)	-	-	16.67 (1)	-
9-11	10.11 (9)	19.10 (17)	41.57 (37)	23.60 (21)	5.62 (5)	-
12-14	8.51 (4)	31.92 (15)	29.79 (14)	14.89 (7)	8.51 (4)	6.38 (3)
15-17	-	14.29 (1)	42.86 (3)	28.56 (2)	14.29 (1)	-
18-20	15.79 (6)	34.21 (13)	18.42 (7)	23.69 (9)	5.26 (2)	2.63 (1)
21-23	25.00 (2)	25.00 (2)	25.00 (2)	12.50 (1)	12.50 (1)	-
24-72	14.58 (7)	22.92 (11)	22.92 (11)	22.92 (11)	8.33 (4)	8.33 (4)
Total (243)	12.35 (30)	25.51 (62)	30.45 (74)	20.99 (51)	7.41 (18)	3.29 (8)

Row percent distribution
Figures in parentheses indicate number of subjects.

In the majority (76.95%) of children, the postvaccination rise in GMT ranged from 3-5 (8-fold to 64-fold). The maximum rise of GMT 8 (256-fold) was seen in 3.29% children only.

Table-40 gives the association between mean postvaccination rise in measles HAI antibody titre (GMT) and age at vaccination in seroconverted children.

The mean rise in GMT ranged from 3.17 to 4.43 in various age groups. The minimum rise (3.17) was seen in the 6-8 months age group, while the maximum rise (4.43) was seen in the 15-17 months age group.

However, no significant difference was observed in mean rise in GMT within various age groups.

Various investigators have reported a similar trend of increase in postvaccination rise in GMT with increase in age at vaccination (5,24, 72,101, 138,151,202,289).

Agrawal (5) has reported an apparent increase in postvaccination GMT with increase in age in children 6-12 months (14.14 to 23.77).

Dholakia (72) has reported a similar apparent trend of increase in postvaccination GMT in children (9-60 months) ranging from 12.17 to 20.02.

However, Job et al (138) have reported a statistically significant linear relationship between postvaccination rise in GMT values with increase in age. Similarly, in a Latin American study (223), post-vaccination titres increased with increasing age from 6-12 months.

In developed countries, higher postvaccination GMT levels have been reported when measles vaccination was given at or around 15 months of age (202,289).

To conclude, age at vaccination has no influence on postvaccination rise in GMT in seroconverted children.

<u>Effect of prevaccination titre on postvaccination rise in measles HAI antibody titres (GMT)</u>

Table-41 demonstrates the association between prevaccination titre

TABLE-40

DISTRIBUTION OF AND ASSOCIATION BETWEEN MEAN POSTVACCINATION RISE IN MEASLES HAI ANTIBODY TITRES (GMT) AND AGE AT VACCINATION IN CHILDREN (6-72 MONTHS) WHO SEROCONVERTED (FOUR-FOLD RISE)

Age at vaccination (months)	n	GMT		Postvaccination rise in GMT mean ± S.E.	One way anova rise in GMT by age at vaccination
		Prevaccination mean ± S.E.	Postvaccination mean ± S.E.		
6-8	6	0.00 ± 0.00	3.17 ± 0.60	3.17 ± 0.60	
9-11	89	0.21 ± 0.05	4.17 ± 0.11	3.96 ± 0.11	F ratio
12-14	47	0.43 ± 0.11	4.51 ± 0.23	4.08 ± 0.22	1.01
15-17	7	0.00 ± 0.00	4.43 ± 0.37	4.43 ± 0.37	F probability
18-20	38	0.53 ± 0.14	4.32 ± 0.20	3.79 ± 0.22	0.42 - N.S.
21-23	8	0.25 ± 0.16	3.88 ± 0.40	3.63 ± 0.50	
24-72	48	0.56 ± 0.14	4.77 ± 0.20	4.21 ± 0.24	
Total	243	0.36 ± 0.05	4.35 ± 0.07	3.99 ± 0.09	

N. S. = Not significant

TABLE-41

ASSOCIATION BETWEEN POSTVACCINATION RISE IN MEASLES HAI ANTIBODY TITRES (GMT) AND PREVACCINATION TITRES IN CHILDREN (6-72 MONTHS) WHO SEROCONVERTED (FOUR-FOLD RISE)

Group	Pre-vaccination titre	Postvaccination rise in GMT							't' test value
		2	3	4	5	6	8	mean ± S.E.	
a (186)	1:2	5.38 (10)	23.12 (43)	33.33 (62)	25.27 (47)	9.14 (17)	3.76 (7)	4.24 ± 0.09	a vs. b 3.02**
b (29)	1:2	31.03 (9)	24.14 (7)	27.59 (8)	13.79 (4)	-	3.45 (1)	3.41 ± 0.26	b vs. c 1.66 - N. S.
c (25)	1:4	40.00 (10)	40.00 (10)	16.00 (4)	-	4.00 (1)	-	2.88 + 0.19	c vs. d 0.58 - N. S.
d (3)	1:8	33.33 (1)	66.67 (2)	-	-	-	-	2.66 ± 0.33	
Total (243)		12.35 (30)	25.51 (62)	30.45 (74)	20.99 (51)	7.41 (18)	3.29 (8)		

Row percent distribution
Figures in parentheses indicate number of subjects.
** = Significant at P 0.01
N.S.= Not significant

and postvaccination rise in antibody level (GMT) in seroconverted children.

An inverse relationship between prevaccination titres and post-vaccination rise in GMT levels was observed. When comparison was made between groups having less than 1:2 and 1:2 prevaccination titre, a significant difference (p 0.01) was observed in their postvaccination rise in GMT levels. No significant difference was observed in other prevaccination titre groups.

Similar inverse relationship has been reported by Agrawal (5), Dholakia (72) and Katiyar (151).

To summarise the combined results of Table-36 and Table-41, both the seroconversion rate and postvaccination rise in measles antibody level were maximum when prevaccination titre was less than 1:2.

Effect of nutritional status on postvaccination rise in measles HAI antibody titres (GMT)

Table-42 depicts the association between nutritional status and postvaccination rise in antibody level (GMT).

In the present study, it was observed that malnourished children responded as well as their well nourished counterparts to measles vaccination. The difference in postvaccination rise in GMT was found to be non-significant.

Similar observations have been reported by Agrawal (5) and Dholakia (72).

Hence, malnutrition is not a contra-indication for measles vaccination and a satisfactory rise in antibody levels is observed in malnourished children following measles vaccination.

Effect of sex on postvaccination rise in measles HAI antibody titres (GMT)

Table-43 describes the association between sex and postvaccination rise in antibody level (GMT).

TABLE-42

ASSOCIATION BETWEEN POSTVACCINATION RISE IN MEASLES HAI ANTIBODY TITRES (GMT) AND NUTRITIONAL STATUS[a] IN CHILDREN (6-72 MONTHS) WHO SEROCONVERTED (FOUR-FOLD RISE)

PEM[a] grade	Postvaccination rise in GMT 2	3	4	5	6	8	Oneway anova rise in GMT by PEM grades[a]
0 (125)	13.60 (17)	23.20 (29)	30.40 (38)	19.20 (24)	10.40 (13)	3.20 (4)	
I (72)	8.33 (6)	23.61 (17)	33.33 (24)	27.78 (20)	6.95 (5)	-	F ratio 1.62
II (34)	14.71 (5)	29.41 (10)	23.53 (8)	20.59 (7)	-	11.76 (4)	F Probability 0.19 - N.S.
III+IV (12)	16.67 (2)	50.00 (6)	33.33 (4)	-	-	-	
Total (243)	12.35 (30)	25.51 (62)	30.45 (74)	20.99 (51)	7.41 (18)	3.29 (8)	

Row percent distribution
(a) = As per IAP Classification (Annexure : 2)
Figures in parentheses indicate number of subjects.
N.S. = Not significant

TABLE-43

ASSOCIATION BETWEEN POSTVACCINATION RISE IN MEASLES HAI ANTIBODY TITRES (GMT) AND SEX

IN CHILDREN (6-72 MONTHS) WHO SEROCONVERTED (FOUR-FOLD RISE)

Sex	Postvaccination rise in GMT							't' test value
	2	3	4	5	6	8	Mean ± S.E.	
Male (144)	10.41 (15)	22.92 (33)	34.03 (49)	22.92 (33)	7.64 (11)	2.08 (3)	4.03 ± 0.10	0.54 - N.S.
Female (99)	15.15 (15)	29.29 (29)	25.25 (25)	18.18 (18)	7.07 (7)	5.05 (5)	3.93 ± 0.15	
Total (243)	12.35 (30)	25.51 (62)	30.45 (74)	20.99 (51)	7.41 (18)	3.29 (8)		

Row percent distribution
Figures in parentheses indicate number of subjects.
N.S. = Not significant

Sex was found to have no influencing role on rise in antibody levels (GMT) following vaccination which is in conformity with studies by Agrawal (5) and Dholakia (72).

The persistence of postvaccination antibody response has two patterns (188). In closed populations, there is a progressive decrease in antibody levels (41,172). However, in open populations, like in India, the level of antibody remains high, presumably due to anamnestic responses to repeated subclinical exposures to wild virus (172).

To summarise, the Seroconversion Study highlighted the following points-

1. Seroconversion rates were significantly lower in children vaccinated at $<$ 9 months of age as compared to those in children vaccinated at $\geq$ 9 months of age.
2. Postvaccination rise in antibody levels (GMT) in seroconverted children was similar in all the age groups.
3. Seroconversion rates were significantly higher in children with prevaccination titres $\leq$ 1:2 as compared to those in children with prevaccination titres $\geq$ 1:4 (Fig.12).
4. Postvaccination rise in antibody titre (GMT) was significantly higher with prevaccination titres $<$ 1:2 as compared to that in children with prevaccination titres $\geq$ 1:2 (Fig. 13).
5. Nutritional status and sex of children had no impact on seroconversion rates.
6. Age at vaccination, nutritional status and sex of children had no influence on postvaccination rise in antibody titres (GMT).

FIGURE-12

SEROCONVERSION RATES ACCORDING TO PREVACCINATION MEASLES HAI ANTIBODY TITRES AND AGE AT VACCINATION IN CHILDREN (0-72 MONTHS)

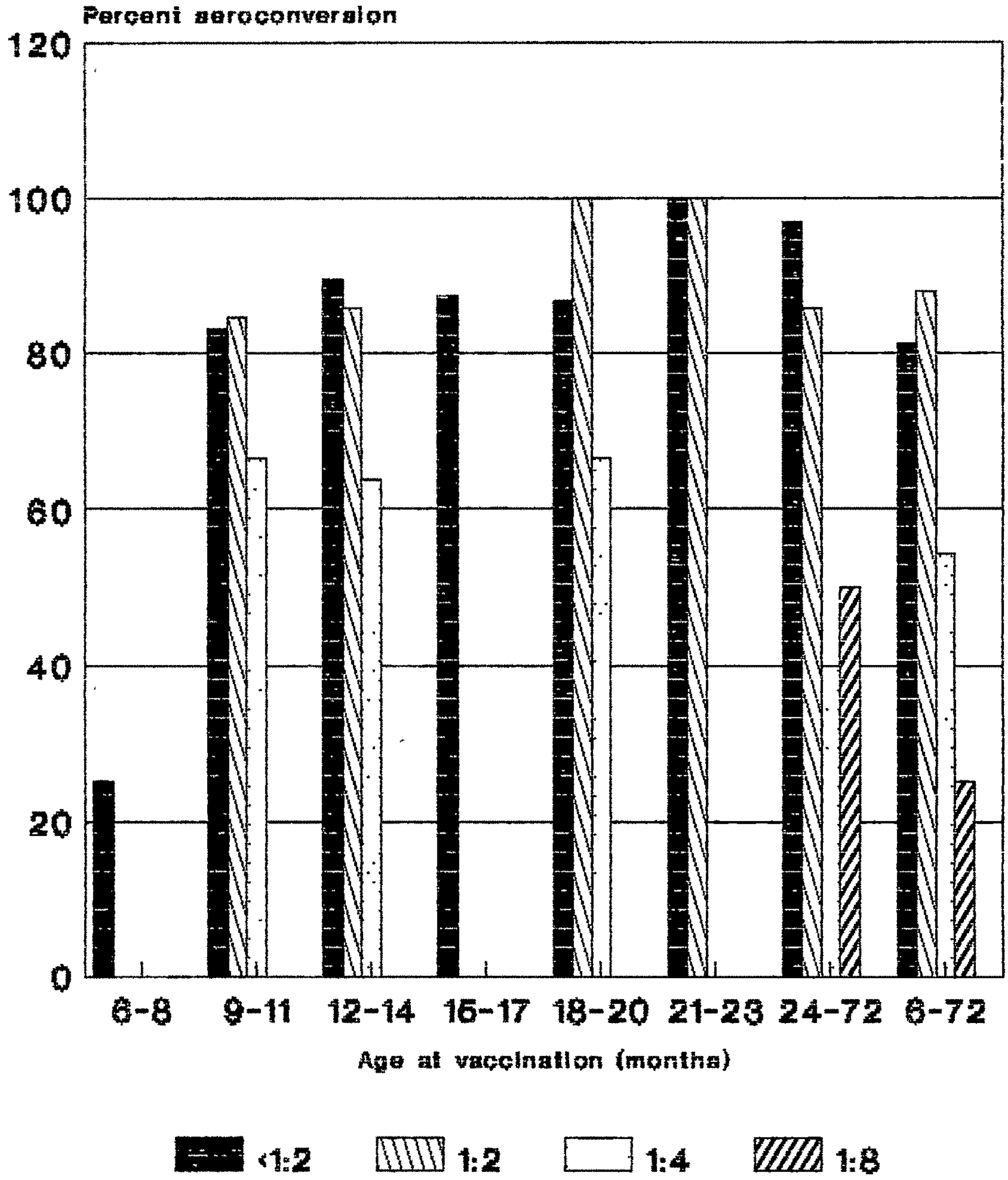


FIGURE-13

POSTVACCINATION RISE IN MEASLES HAI ANTIBODY TITRES (GMT)
IN CHILDREN (0-6 MONTHS) WHO SEROCONVERTED (FOUR-FOLD RISE)