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A Study on the Role of Haptoglobin in Haemolytic Disease of the Newborn

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ABSTRACT The present study attempts to find the role of Haptoglobin in the hemolytic disease of the newborn (HDN) , to ascertain the selective advantage of HP*1 over HP*2 , due to greater binding capacity of hemoglobin of the former; and to find the association of Haptoglobin with ABO blood group system. 71 children (37 – male; 34 – female) with HDN were studied along with their parents. Distribution of Haptoglobin according to various mother-child combinations was studied. Mothers of HDN patients showed an excess frequency of 'O' alleles and children with HDN, showed a significant excess of A_1 and A_2 alleles compared to those of control newborns. Among the mothers of HDN children 'd' allele was frequent, but notably absent in father and children. It was seen that frequency of HP*1 allele, was more among HDN children with double incompatible mother-child combinations, than those among the HDN patients with double compatible mother-child combinations. Further follow up of the HDN patients without detectable Haptoglobin types required exchange transfusion, but those with detectable Haptoglobin types did not require exchange transfusion irrespective of mother-child combination. Trend towards protective effects of HP in mean hemoglobin level and other parameters of HDN patients was evident.

INTRODUCTION

Since the publication of Kirk (1968) and Giblett (1969) significance of Haptoglobin groups (HP) in disease, was the subject matter for number of studies with regard to the role of these protein groups in hemolytic disorders of the new born (Laurell and Nyman 1957; Nyman 1959, 1960; Owen et al. 1959, 1960, 1964; Jayle et al. 1962; Laurell and Gronvall 1962). Decrease in the level of HP in various hemolytic disorders was noted by Curtain et al. (1965), Gupte et al. (1975), Padma et al. (1980), Murty and Padma (1984); Padma and Valli (1988).

Kirk at el. (1970) in an extension to the finding of Ritter and Hinkelmann (1966) on higher frequencies of *HP*1* (Bandyopadhyay 1993,1994) alleles among the children born with ABO incompatible parental and mother child combination than that of ABO compatible combinations, introduced the idea of selective advantage of *HP*1* alleles than *HP*2* alleles for its greater binding capacity of hamoglobin in haemolytic disease of the newborns (HDN) arising due to ABO incompatibility (Levine 1943; Halbrecht 1944; Polayes 1945; Mollison 1967; Gold and Buttler 1972; Banerjee 1989). Kirk (1971) in subsequent publications, however, reported the reality of the phenomenon of ABO- HP interaction effects as noted originally by Ritter and Hinkelman (1966) but, the idea of better conservation of released hemoglobin (Hb) in increased red cell destructions due to ABO incompatibility in infants by *HP*1* than *HP*2* allele as introduced earlier, appeared to be some how difficult to understand.

In search for an alternative mechanism for the above mentioned phenomenon, Vana and Steinberg (1975) noted that, the higher incidence of *HP*1* in ABO incompatibility than in ABO compatibility was not based on incompatibility or compatibility of blood groups, but rather on unexplained association of *HP*1* alleles with ABO alleles. Similar phenomenon was also reported from Australia (Mitchell et al. 1988) and India (Bandyopadhyay 1992)

However interpretations of Kirk et al. (1970), Kirk (1971), Vana and Steinberg (1975), Mitchell et al. (1988) and Bandyopadhyay (1992) were based mainly on population studies, and actual case studies for HP in HDN due to ABO incompatibility between mother and child arising out of incompatible matings were rarely taken into consideration (Gupte et al. 1975). With above contentions, studies on HP- ABO and HP-Rh (D) incompatibility interactions in actual cases of HDN thus appeared to be essential to understand the implication of HP in haemolytic disorders like HDN due to feto-maternal blood group

incompatibilities.

MATERIALS AND METHODS

The data (blood of 71 children diagnosed with HDN; 37 – male and 34 – female, and their parents; 71 mothers and 71 fathers) for the present study was collected from the Genetic laboratory and Department of Pediatrics of Vivekananda institute of Medical Sciences, Ramakrishna Mission Seva Pratishthan. ABO and Rh (D) blood groups have been done by agglutination test (Prokop et al. 1961) using standard antisera. Serum bilirubin level has been determined by Diazo reaction, while Hemoglobin was verified by Cyanomythemoglobin method. Haptoglobin groups were identified by PAGE (Polyacrylamide Gel Electrophoresis) method (Hoppe et al.1972 and Pastewka et al. 1973) with slight modifications. Allele frequencies for ABO, Rh(D) blood groups and Haptoglobin groups were computed by Maximum Likelihood Estimation (Vogel and Motulski, 1998, Mourant et al. 1976). Data analysis was done by Microsoft Excel and SPSS on windows version 6.0. Other statistical analysis was done following Madrigal (1998)

RESULTS AND DISCUSSION

Distribution of A1A2BO groups and their gene frequencies among the children with HDN and their parents as presented in table 1, showed heterogeneity between the mother and the father of the children with HDN for the distribution of A1A2BO blood groups (Chi^2= 21.58; 5 d.f.; p< 0.001); this was due to high frequencies of *O* allele among the mother compared to those among the father. Incidence of *A1* allele among the father was also found to be much higher than that among the mother. No heterogeneity in the distribution of A1A2BO blood groups between the male and female children with HDN could be seen (Chi^2 = 0.58, 5 d.f., p> 0.50). Contrary to that, heterogeneity in the distribution of A1A2BO blood groups between parents and children with HDN could be well marked (Chi^2= 18.21, 5 d.f., p< 0.01). When the distribution of A1A2BO blood groups among the parents of the children with HDN was compared with that among parents of the newborn taken as control population, heterogeneity between the two groups of father (Chi^2= 23.87, 5 d.f., p< 0.001) was well marked due to very high frequency of A_1 alleles among the former compared to that among the later. Mothers of the HDN patients also showed higher frequencies of *O* alleles than those of the mother of the newborns taken as control (Chi^2= 10.04, 5 d.f., p> 0.05). Children with HDN showed significantly excess of *A1* and *A2* alleles compared to those of the newborns (Chi^2= 47.41, 5 d.f., p< 0.001) when the later group was taken as control.

Distribution of RH (D) blood groups among the children with HDN and their parents as presented in table 2, showed the presence of d allele among the mother only, while among the father and among the children with HDN it was marked by its absence. Significant heterogeneity

Table 1: Distribution and allele frequency of A1A2BO blood groups in HDN and their parents

		Blood Groups						*Total (N)*	*Allele*				
		O	*A1*	*A2*	*B*	*A1B*	*A2B*		*A1*	*A2*	*B*	*O*	Chi^2_5
Mother	N	37	9	2	20	2	1	71	0.080	0.023	0.177	0.718	
	%	52.1	12.6	2.82	28.1	2.82	1.40						
Father	N	15	29	1	23	3	-	71	0.239	0.039	0.211	0.557	
	%	21.1	40.8	1.40	32.3	4.24							21.58*
Male	N	9	9	6	13	-	-	37	0.135	0.103	0.232	0.557	
(HDN)	%	24.3	24.3	16.2	35.1								
Female	N	11	7	5	11	-	-	34	0.112	0.089	0.182	0.615	
(HDN)	%	32.3	20.5	14.7	32.3								0.58
Parents	N	52	38	3	43	5	1	142	0.614	0.014	0.190	0.631	
	%	36.6	26.7	2.11	30.2	3.52	0.71						
HDN	N	20	16	11	24	-	-	71	0.214	0.096	0.193	0.585	
Children	%	28.1	22.5	15.4	33.8	-	-						18.21*

* significant at 1% level.

Table 2: Distribution and allele frequency of RH(D) blood groups in HDN and their parents

		RhD	*Rd D-*	*Total (N)*	*D*	*d*
Mother	N	47	24	71	0.4186	0.5814
	%	66.20	33.80			
Father	N	71	-	71	1.0000	-
	%	100.00	-			
Male (HDN)	N	37	-	37	1.0000	-
	%	100.00	-			
Female (HDN)	N	341	-	34	1.0000	-
	%	100.00	-			
Parents	N	118	24	142	0.5889	0.4111
	%	83.10	16.90			
HDN Children	N	71	-	71	1.0000	-
	%	100.00				

Table 3: Distribution and allele frequency of haptoglobin groups in HDN and their parents

		0-0	*1-1*	*2-1*	*2-2*	*Total*	*HP*1*	Chi^2_2
Mother	N		2	15	54	71	0.1338	
	%		2.82	21.12	76.06			0.35
Father	N		2	18	51	71	0.1549	p>0.50
	%		2.82	25.35	71.83			
Male (HDN)	N	11	2	7	17	37	0.2115	
	%	29.73	5.41	18.92	45.96			0.49
Female (HDN)	N	12	3	5	14	34	0.2500	p>0.50
	%	35.29	8.82	14.71	41.17			
Parents	N	-	4	33	105	142	0.1443	
	%		2.82	23.24	73.94			
HDN Children	N	23	5	12	31	71	0.2292	4.86*
	%	32.39	7.04	16.91	43.66			0.10<p>0.05

(Chi^2= 70.70, 1 d.f., p< 0.001) between the mother of the children with HDN and mother of the newborns for the distribution of Rh (D) blood groups was found due to very high frequencies of d alleles among the former (0.5814) compared to those among the later (0.2449).

Distribution of HP groups, table 3, showed no heterogeneity between the father and the mother of the HDN patients (Chi^2= 0.35, 2 d.f. p> 0.50) and between the male and female children with HDN (Chi^2 = 0.49, 2d.f, p> 0.50). A trend towards the heterogeneity in the distribution of HP groups (Chi^2 = 4.86, 2 d.f., 0.10< p> 0.05) between the children with HDN and their parents was marked due to higher frequencies of HP*1 alleles (Chi^2 = 3.73, 1 d.f., 0.10< p> 0.05) in the children with HDN than in their parents. In the distribution of HP groups between the parent of the newborns and the parent of HDN patients no significant difference (Chi^2 = 1.27, 2 d.f., p> 0.20) could be found.

In the incidence of parental ABO incompatibility of the newborn (69.90%) and the parent of the HDN patients (69.10%) were found to be very much closer to each other. Incidence of Rh (D) incompatibility among the parent of the children with HDN (33.80%) was found to be significantly higher (Chi^2 = 46.29, 1 d.f. p< 0.001) than that among the parent of control newborns (8.23%).

A comparative picture of HP distribution among the children with HDN and among the new borns for ABO and in Rh (D) mother-child combinations has been presented in table 4 and 5 respectively. ABO incompatible mother-child combinations (Table 4) was found to be significantly higher in the children with HDN (Chi^2 = 31.46, 1 d.f. P < 0.001) than that in the newborns. Detectable HP showed although a higher incidence in the HDN patient with ABO incompatible than ABO compatible mother-child combinations, but the differences between these two incidences was not statistically significant (Chi^2 = 0.74, 1 d.f., P> 0.30). Frequencies of *HP*1* gene was also found to be higher in ABO incompatible than in ABO compatible mother-child combinations; but, the distribution of HP in the two

Table 4: Distribution and allele frequency of haptoglobin groups in HDN and control newborns, according to ABO mother-child combination

Category	*Mother-child Combinations*		*0-0*	*1-1*	*2-1*	*2-2*	*Total (N)*	*HP*1*	*Chi^2_2*
HDN	Compatible	N	14	2	5	17	38	0.1875	0.82
		%	36.84	5.26	13.16	44.74	53.53		p>0.50
HDN	Incompatible	N	9	3	7	14	33	0.2708	
		%	27.27	9.09	21.22	42.42	46.47		
Total HDN	Compatible &	N	23	5	12	31	71	0.2292	
	Incompatible	%	32.39	7.05	16.90	43.66			
Newborns	Compatible	N	472	8	69	216	765	0.1451	
		%	61.70	1.04	9.02	28.24	76.50		1.18
Newborns	Incompatible	N	105	6	32	92	235	0.1692	p>0.30
		%	44.68	2.55	13.62	39.15	23.50		
Total Control	Compatible &	N	577	14	101	308	1000	0.1524	
Newborns	Incompatible	%	57.70	1.40	10.10	30.80			

Chi^2_2 = Total HDN vs Total newborns (Control) = 5.82; $0.10 < p > 0.05$.

Table 5: Distribution and allele frequency of haptoglobin groups in HDN and control newborns, according to RH (D) mother – child combination

Category	*Mother-child Combinations*		*0-0*	*1-1*	*2-1*	*2-2*	*Total (N)*	*HP*1*	*Chi^2_2*
HDN	Compatible	N	14	3	6	24	47	0.1818	
		%	29.79	6.38	12.77	51.06			
HDN	Incompatible	N	9	2	6	7	24	0.3333	3.23
		%	37.50	8.33	25.00	29.17			P>0.100
Total HDN	Compatible &	N	23	5	12	31	71	0.2292	
	Incompatible	%	32.39	7.05	16.90	43.66			
Newborns	Compatible	N	544	10	99	287	940	0.1502	
		%	57.87	1.06	10.53	30.53			
Newborns	Incompatible	N	33	4	2	21	60	0.1852	14.91
		%	55.00	6.67	3.33	35.00			P>0.01
Total Control	Compatible &	N	577	14	101	308	1000	0.1524	
Newborns	Incompatible	%	57.70	1.40	10.10	30.80			

Chi^2_2 = Total HDN vs Total newborns (Control) = 5.82, $0.10 < p > 0.05$.

groups of HDN patients, ABO compatible and ABO incompatible was not statistically significant ($Chi^2 = 0.82$, 3 d.f., $p > 0.30$). Significantly higher frequencies of detectable HP groups were also found in the newborns ($Chi^2 = 20.73$, 2 d.f., $p < 0.001$). A trend towards the heterogeneity in the distribution of detectable HP types between ($Chi^2 = 5.82$, 2 d.f., $0.10 < p > 0.05$) the newborn and the HDN patients was evident due to higher frequencies of HP*1 in the HDN patients ($Chi^2 = 3.78$, 1 d.f., $0.10 < p > 0.05$) than in the newborns.

Mother-child combination for Rh (D) blood groups in the HDN patients and in the newborns as presented in table 5, showed although higher incidences of HP*1 alleles (0.3333) in Rh (D) incompatibility than in Rh (D) compatibility (0.1818) among the HDN patients but not up to the level of statistical significance ($Chi^2 = 2.68$, 1 d.f. $p < 0.10$). No significant difference between the distribution of HP groups ($Chi^2 = 3.23$, 2 d.f., $p > 0.10$) of the HDN patients with Rh (D) incompatibility and Rh (D) compatibility in their mother-child combinations, could be seen. Significant difference ($Chi^2 = 5.82$, 2d.f., $0.10 < p > 0.05$) between the HDN patients and the control newborns for the distribution of HP was noted, due to higher incidences of HP 1-1 genotype in the former than the later.

When the distribution of Haptoglobin among the HDN patients for ABO and Rh (D) mother-child combinations taken together was considered in table 6, a trend towards the heterogeneity between the HDN patients with ABO and Rh (D) incompatibility and the HDN patients with ABO and Rh (D) compatibility for the distribution of HP groups, ($Chi^2 = 5.10$, 2 d.f., $0.10 < p > 0.05$)

Table 6: Distribution and allele frequency of haptoglobin groups in HDN according to their ABO and Rh (D) mother-child combination

Mother-child Combinations		*0-0*	*1-1*	*2-1*	*2-2*	*Total*	*HP*1*	*Chi^2_2*
ABO [C] Rh (D) [C]		6	-	1	11	18	0.0417	
	Exp		0.02	0.96	11.02			7.90
	%	33.33	-	5.56	61.11			P>0.05
ABO [C] Rh (D) [IC]		8	2	4	6	20	0.3333	
	Exp		1.30	5.40	5.30			0.47
	%	40.00	10.00	20.00	30.00			p>0.05
ABO [IC] Rh (D) [C]		8	3	5	13	29	0.2619	
	Exp		1.40	8.10	11.50			2.45
	%	27.59	10.34	17.24	44.83			p>0.05
ABO [IC] Rh (D) [IC]		1	-	2	1	4	0.3333	
	Exp		0.3	1.3	1.4			
	%	25.00	-	50.00	25.00			

Chi^2_2 = ABC [C] Rh(D) [C] vs ABO [IC] Rh (D) [IC] = 5.10; $0.10 < p > 0.05$.
Exp = Expected; C=Compatible; IC=Incompatible

incidences of *HP*1* alleles among the HDN patients with double incompatible mother-child combinations than those among the HDN patients with double compatible mother-child combinations was found.

Result of the follow up study during the stay of the HDN patients in the hospital, as presented in table 7, on the background of their ABO and Rh (D) mother-child combinations, showed no significant difference between the mean birth weight of the HDN patients classified according to the availability of detectable HP groups and compatibility and incompatibility for ABO and Rh (D) mother-child combinations. When the data on mean birth weight (in grams) of the HDN patients were compared with those of the newborns (Table 7a) on the basis of availability and non-availability of detectable HP types in the compatible and incompatible ABO and Rh (D) mother-child combinations, no significant differences between the mean birth weight of the HDN patients and the newborns in each case of the class, excepting in ABO compatible mother-child combinations where the newborns with detectable HP groups , showed significantly higher ($t = 4.83, p<0.05$) mean birth weight (2712.03 ± 28.00 gms) than that of the newborns (2559.20 ± 14.70 gms) with undetectable HP groups (HP 0-0). It is interesting to note that, in spite of the absence of significant difference between the mean birth weight of the HDN patients as well as of the newborns in the compatible and incompatible mother-child combinations, a trend towards the lower birth weight of the babies with non-detectable HP in ABO and Rh (D) incompatible than in compatible mother-child combinations could be seen.

Mean Hb level (Table 7a,b) of the HDN patients with detectable HP types was found to be higher than that of HDN patients without detectable HP in ABO compatible and incompatible combinations as well as in Rh (D) compatible and incompatible mother-child combinations was found to be significantly lower ($t = 8.48, p<0.10$) than that of the HDN patients with ABO compatible mother-child combinations. The trend was almost similar for the Rh (D) HDN patients in Rh (D) incompatible and Rh (D) compatible mother-child combinations, although difference between the levels of HP was not statistically significant ($t = 0.72, p>0.05$). A reverse trend towards the higher levels of bilirubin was noted among the patients with ABO incompatibility than those of the patients with ABO compatibility in the mother-child combinations, although the difference between the above-mentioned levels of bilirubin was not statistically significant. Almost similar trend towards the increased levels of bilirubin among the HDN patients with Rh (D) incompatibility compared to that among the HDN patient with the RH (D) compatibility in mother-child combination was noted. It was interesting to note that serum bilirubin levels of the HDN patients decreased with the availability of detectable HP in all the ABO and Rh (D) mother-child combinations.

With regard to the clinical management of HDN patients pertaining to exchange transfusion,

Table 7a: Available details of HDN patients, according to detectable and undetectable haptoglobin types in different ABO and Rh (D) mother-child combinations

	ABO Mother-Child Combinations						*Rh [D] Mother-Child Combinations*					
	ABO compatible			*ABO incompatible*			*Rh [D] compatible*			*Rh [D] incompatible*		
	HP-0	*with HP*	*Total*	*HP-0*	*with*	*Total*	*HP-0*	*with*	*Total*	*HP-0*	*with HP*	*Total*
Number	*14*	*24*	*38*	*9*	*24*	*33*	*14*	*33*	*47*	*9*	*15*	*24*
Mean birth weight in grams	2562.71 ±135.55	2553.97 ±101.80	2558.66 ±82.59	2575.24 ±172.43	2521.42 ±97.41	2534.88 ±84.82	2549.23 ±142.99	2539.69 ±92.33	2544.97 ±84.08	2498.72 ±169.28	2502.43 ±159.29	2509.57 ±112.31
Mean Haemoglobin [gm/100 ml]	110.78 ±1.89	114.62 ±1.72	112.26 ±1.39	103.82 ±1.54	105.29 ±1.73	104.37 ±1.28	106.92 ±1.73	107.29 ±1.49	106.81 ±1.79	104.93 ±1.89	105.74 ±1.29	105.23 ±1.27
Mean bilirubin [mg/100 ml]	10.73 ±1.26	8.84 ±1.17	9.79 ±1.21	13.46 ±2.99	10.75 ±1.23	12.11 ±2.11	14.69 ±1.94	11.78 ±1.21	12.44 ±1.09	16.59 ±1.11	15.72 ±1.74	14.47 ±1.28
Exchange transfusion %	8 57.14	4 16.67	12 31.58	9 100.00	19 79.17	28 84.85	14 100.00	18 54.55	32 68.08	9 100.00	9 60.00	18 75.00
Phototherapy %	2 14.29	7 29.17	9 23.68	- -	3 12.50	3 9.09	- -	8 24.24	8 21.28	- -	4 26.67	4 16.66
Survivality %	8 57.15	17 70.83	25 65.79	4 44.45	17 70.84	21 63.64	5 35.71	29 87.88	34 72.34	3 33.34	9 60.00	12 50.00
Mortality due to kernicterus %	5 35.71	4 16.67	9 23.68	3 33.33	5 20.83	8 24.24	6 42.86	3 9.09	9 19.14	5 44.45	3 20.00	8 33.33
Mortality other than kernicterus %	1 7.14	3 12.50	4 10.53	2 22.22	2 8.33	4 12.12	3 21.43	1 3.03	4 4.26	1 11.11	3 20.00	4 8.33
HP*1			0.1875			0.2708			0.1818			0.3333

Table 7b: Available details of HDN patients, according to detectable and undetectable haptoglobin types with ABO and Rh [D] mother-child combinations

	ABO compatible Rh [D] Compatible			*ABO compatible Rh [D] incompatible*			*Rh [D] incompatible Rh [D] Compatible*			*Rh [D] incompatible Rh [D] incompatible*		
	HP-0	*with HP*	*Total*	*HP-0*	*with HP*	*Total*	*HP-0*	*with HP*	*Total*	*HP-0*	*with HP*	*Total*
Number	*6*	*12*	*18*	*8*	*12*	*20*	*8*	*21*	*29*	*1*	*3*	*4*
Mean birth weight	2553.97	2551.26	2552.62	2530.71	2532.88	2541.39	2562.33	2530.66	2551.23	2500.00	2508.67	2503.65
± s.e. in grams	±192.37	±172.33	±182.98	±204.31	±189.41	±193.77	±216.35	±94.99	±149.73		±278.64	±278.64
Mean Haemoglobin	111.04	110.39	110.92	107.38	109.34	108.33	104.52	106.39	103.24	101.33	107.43	104.77
[gm/100 ml]	±1.99	±1.73	±1.78	±1.81	±1.91	±1.83	±2.31	±1.61	±1.83		±1.31	±1.31
Mean serum	16.33	15.32	15.32	16.34	14.79	16.75	14.22	12.75	13.98	19.34	12.33	17.85
bilirubin	±1.87	±1.74	±1.83	±1.93	±1.77	±1.84	±1.96	±1.39	±1.54		±2.32	±2.32
Exchange	4	5	9	7	7	14	8	17	25	-	2	2
transfusion %	66.67	41.67	50.00	87.50	58.33	70.00	100.00	80.95	86.21		66.67	50.00
Phototherapy	2	3	5	-	3	3	-	4	4	-	-	-
%	33.33	25.00	27.78		25.00	6.66		19.04	13.79			
Survivality	2	9	11	4	8	12	5	14	19	1	3	4
%	33.33	75.00	61.11	50.00	66.67	60.00	62.50	66.67	65.52	100.00	100.00	100.00
Mortality due to	2	2	4	3	3	6	3	4	7	-	-	-
kernicterus %	33.33	16.67	22.22	37.50	25.00	30.00	39.50	19.05	24.14	-	-	-
Mortality other than	2	1	3	1	1	2	-	3	3	-	-	-
kernicterus %	33.33	8.33	16.67	12.50	8.33	10.00	-	14.29	10.34	-	-	-
HP*1			0.0417			0.3333			0.2619			0.3333

much more necessity of it was noted for the patients with undetectable HP types, irrespective of their status of ABO and Rh (D) mother-child combinations. Although significantly higher (t = 5.44) number of patients for exchange transfusion were noted among the HDN patients in ABO incompatible than in ABO compatible mother-child combinations, but it was interesting to note that out of 24 HDN patients with detectable HP in ABO incompatible mother-child combinations, 19 (79.17%) required exchange transfusion compared to all of the 9 HDN patients without detectable HP in this group, required exchange transfusion. A picture identical to that as noted among the HDN patients in ABO mother-child combinations was found among the HDN patients with Rh (D) mother-child combination. Significantly higher (t = 2.74) number of patients with Rh (D) incompatible mother-child combination required exchange transfusion; out of 15 HDN patients with detectable HP, 9 required exchange transfusion, while all of the 9 patients without detectable HP required exchange transfusion. It was further interesting to note that, in ABO incompatible as well as in Rh (D) incompatible mother-child combinations, 12.50% and 26.67% of the HDN patients respectively with detectable HP types in photo therapy was applied instead of exchange of transfusion, while none of the patients having incompatible blood group combinations with their mother and without detectable HP responded to photo therapy. In survivability and mortality of the HDN patients due to Kernicterus, association between the above mentioned events and detectable HP was noted. Higher frequencies of survivability were noted among HDN patients with detectable HP. In ABO incompatible mother-child combinations, a lesser frequency of mortality due to Kernicterus (24.24%) compared to that in Rh (D) incompatible mother-child combination was noted. Mortality of HDN patients due to other disease, apart from Kernicterus, showed equal frequencies in ABO and Rh (D) combinations (11.26%). The main cause for mortality of the HDN patients other than Kernicterus, infection to the respiratory tract, asphyxia, septititis and haemangeoma etc. were found to be responsible.

In spite of the smallness of the data, availability of HP was noted in lower birth weight among the HDN patients with double incompatibility than that of the patient with double compatible mother-child combinations. Trend towards protective effects of HP in mean Hb level, serum bilirubin level, exchange transfusion, photo therapy for the HDN patients with double incompatibility was to some extent evident. Further work, with more data, however, is necessary to have the complete picture of the HP interactions in the HDN due to foeto-maternal blood group incompatibilities.

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