Bilirubin Course among Newborns with Glucose-6-Phosphate Dehydrogenase Enzyme Reduced Activity

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Objective: To evaluate the course of jaundice in newborns with G6PD reduced activity compared to G6PD normal activity.

Design: A Prospective Study.

Setting: Salmaniya Medical Complex and Jidhafs Maternity Hospital, Bahrain.

Method: This is a prospective study on newborns from May to September of 2015. Total Serum Bilirubin (TSB) was measured from day one of life to day seven for all neonates. G6PD activity was documented from the records.

Results: One hundred twenty-five children were included in the study; 71 (56.8%) were newborns with normal G6PD activity and 54 (43.2%) were G6PD reduced activity. The mean TSB was significantly higher in newborns with G6PD reduced activity 11.23±3.50 mg/dl compared to newborns with G6PD normal activity 9.52±4.16 mg/dl (P-value 0.001).

The mean TSB on day one for newborns with G6PD reduced activity was higher compared to newborns with G6PD normal activity; 6.37±6.76 mg/dl and 1.82±1.94 mg/dl respectively (P-value 0.078).

Conclusion: The course of hyperbilirubinemia in children with G6PD reduced activity was different compared to children with G6PD normal activity. The mean TSB was significantly higher in newborns with G6PD reduced activity. A bilirubin level of 6mg/dl during the first neonatal day could be an indicator for the presence of G6PD reduced activity in the newborn.

Bahrain Med Bull 2016; 38 (3): 135 - 138

Neonatal jaundice is a common condition in newborns[1,2]. It affects approximately 60% of term newborns and 80% of premature neonates[1-6]. Neonatal jaundice is a transient physiologic condition that is mainly related to immaturity of the newborn liver conjugating enzymes which normally enhance the excretion of bilirubin. Physiologic jaundice usually does not cause any complications to the newborn[1-7]. On the other hand, Glucose-6-Phosphate Dehydrogenase (G6PD) reduced activity could cause significant hyperbilirubinemia in the newborn which may lead to encephalopathy and kernicterus[8-12].

G6PD is the most common enzymopathy of the red blood cell. Four hundred million people worldwide are estimated to have this disorder[8]. According to the US Registry of Kernicterus, 21% of cases of neonatal kernicterus were reported in neonates with G6PD reduced activity[9]. The early recognition and treatment of newborn hyperbilirubinemia is the main approach set by the 2004 American Academy of Pediatrics (AAP) guidelines to prevent kernicterus[4,7,9-18].

The aim of this study is to evaluate the course of jaundice in G6PD reduced activity newborns in Bahrain compared to normal G6PD activity.

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METHOD

This is a prospective study on newborns from May to September 2015. The sample was randomly selected; all newborns in the postnatal wards on alternate weeks were included. Informed consent was obtained from the mothers. The personal characteristics were documented. Daily total serum bilirubin measurements were obtained up to neonatal day seven.

The data was entered and analyzed using Statistical Package SPSS Version 20.0. Quantitative variables are presented as Mean ± SD, and qualitative variables are presented as counts and percentages. Odds ratio and Chi-Square were used to measure the association between variables. P-value < 0.05 was considered statistically significant.

RESULT

One hundred twenty-five newborn infants were included in the study; 71 (56.8%) had normal G6PD activity and 54 (43.2%) had G6PD reduced activity. Forty-eight of the newborns with normal G6PD activity and all the newborns with the G6PD reduced activity were Bahrainis; therefore, one hundred two (81.6%) were Bahrainis. In the G6PD normal activity group, 33 (26.4%) were males and 37 (29.6%) of the G6PD reduced activity group were males. Twenty-six (20.8%) of the G6PD normal activity group were exclusively breast fed, while 28 (22.4%) of the G6PD reduced activity group were exclusively breast fed, see table 1.

Table 1: Personal Characteristics

		G6PD Activity						
		Normal (71)		Reduced (54)				
		No.	%	No.	%	Total	%	P-value
Nationality	Bahraini	48	38.4	54	43.2	102	81.6	
	Non Bahraini	23	18.4	0	0.0	23	18.4	0.0001
	Total					125	100	
Gender	Male	33	26.4	37	29.6	70	56	
	Female	38	30.4	17	13.6	55	44	0.014
	Total					125	100	
Feeding Pattern	Breast Feeding	26	20.8	28	22.4	54	43.2	
	Formula and mixed	45	36	26	20.8	71	56.8	0.089
	Total					125	100	

The G6PD normal activity group had 139 TSB readings. The maximum TSB reading in this group was 19.35 mg/dl. The G6PD reduced activity group had a total of 113 TSB readings and the maximum reading recorded for this group was 21.35 mg/dl, see table 2.

Table 2: TSB of Newborns with G6PD Normal Activity and G6PD Reduced Activity

	Total Serum Bilirubin					
G6PD	N. Test	Mean	SD	Min	Max	Range
Normal	139	9.52	4.16	0	19.35	19.35
Reduced	113	11.23	3.50	0.47	21.35	20.88
Total	252	10.29	3.96	0	21.35	21.35

The mean bilirubin level was 11.23 mg/dl for newborns with G6PD reduced activity. On day one, the mean TSB level was 6.37 mg/d. The rate of TSB increase followed a steep line up to day four. It then plateaued for three days and reached the peak TSB level by day seven. It started dropping on day eight. The peak TSB level was 13.50 mg/dl, see table 3 and figure 1.

Table 3: Mean of TSB in Newborns with G6PD Reduced Activity

Day	Total Serum Bilirubin		
	N. Test	Mean	Difference*
1	4	6.37	
2	19	8.54	2.17
3	17	9.61	1.07
4	18	12.63	3.01
5	20	12.85	0.32
6	11	12.84	0.10
7	13	13.50	0.66
8	6	10.92	2.58
9	5	10.34	0.58
Total	113	11.23	

*Difference from previous day

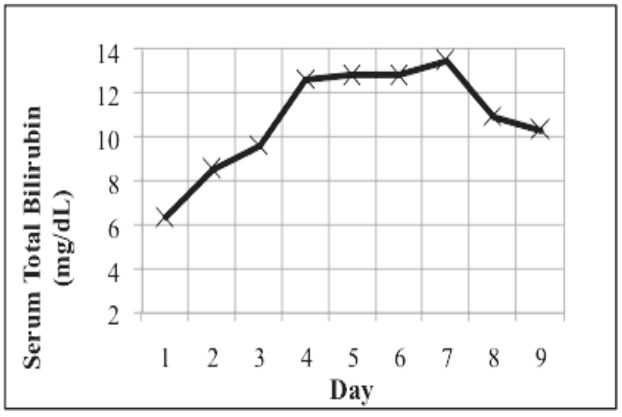

Figure 1: Mean of TSB in Newborns with G6PD Reduced Activity

All infants had a mean bilirubin of 10.29 mg/dl; the mean on day one was 3.42 mg/dl. The rate of increase followed a steep line up to day four and slowed down from day four until it reached its peak on day seven. The level started dropping on day eight. The peak TSB level was 13.18 mg/dl, see table 4 and figure 2.

Table 4: Mean of TSB in Newborns

	Total Serum Bilirubin		
Day	N. Test	Mean	Difference*
1	14	3.42	
2	47	7.58	4.16
3	44	9.06	1.48
4	46	11.50	2.44
5	34	12.33	0.83
6	24	12.72	0.39
7	25	13.18	0.46
8	10	11.33	1.85
9	10	10.77	0.63
Total	252	10.29	

*Difference from previous day

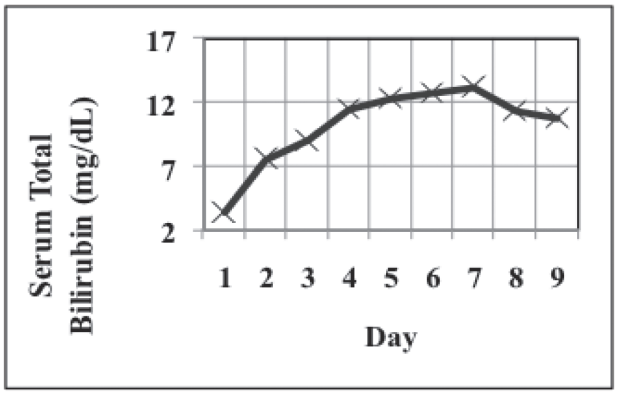

Figure 2: Mean of TSB in Newborns

The mean TSB level was 9.52 mg/dl and the mean TSB level on day one was 1.82 mg/dl for neonates with normal G6PD activity. There was an increase in the TSB level between day one and day two of almost 5 mg/dl. The peak TSB was reached on day seven, and the rate of increase was minimal between the fourth and the seventh day. The peak TSB level was 12.84 mg/dl, see table 5 and figure 3.

Table 5: Mean TSB in Newborns with Normal G6PD Activity

	Total Serum Bilirubin		
Day	**N. Test**	**Mean**	**Difference***
1	9	1.82	
2	28	6.93	5.11
3	26	8.73	1.80
4	28	10.77	2.04
5	14	11.58	0.81
6	13	12.61	1.03
7	12	12.84	0.23
8	4	11.94	0.90
9	5	11.20	0.74
Total	**139**	**9.52**	

*Difference from previous day

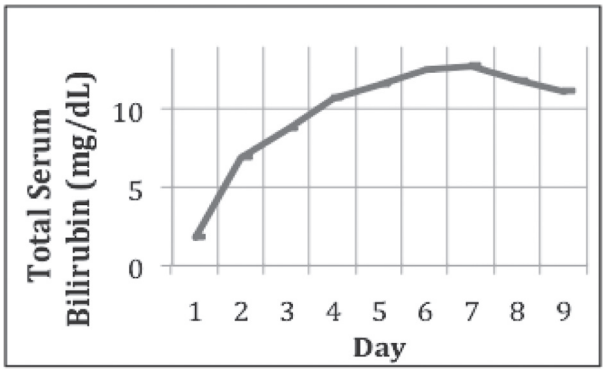

Figure 3: Mean TSB in Newborns with Normal G6PD Activity

DISCUSSION

The course of hyperbilirubinemia in neonates with G6PD reduced activity was slightly different compared to neonates with G6PD normal activity. The mean TSB was significantly higher in newborns with G6PD reduced activity compared to newborns with G6PD normal activity (P-value 0.001). Badejoko et al found that G6PD reduced activity newborns have higher TSB levels during the first week of life compared to newborns with G6PD normal activity (P<0.001)[19].

The mean TSB on day one for newborns with G6PD reduced activity was higher than newborns with G6PD normal activity (6.376.76± mg/dl and 1.821.94± mg/dl, respectively), P-value 0.078.

Newborns with G6PD reduced activity start with high bilirubin level from day one, while newborns with normal G6PD have low TSB level on day one and then increase significantly between day one and day two. In newborns with normal G6PD activity, TSB increases between day one and day two; the mean TSB difference between day one and day two was 5.11 mg/dl.

The average daily increase in TSB for G6PD reduced activity was 2 mg/dl/day, while the average increment per day for neonates with normal G6PD activity was 1.9 mg/dl/day, from day two to day four. The mean daily increment in TSB for G6PD reduced activity was 0.4 mg/dl compared to 0.7mg/dl for neonates with normal G6PD activity, from day four up to day seven. Both groups had almost the same tendency of relatively higher rate of TSB increase between days 2 to 4 up to day seven; both had their peak TSB level on day seven. The peak bilirubin for both groups was not significantly different (13.50±2.83 mg/dl for G6PD reduced activity and 12.843.70± for G6PD normal activity) the P-value was 0.732.

Celik et al found no significant difference between G6PD reduced activity newborns and newborns with G6PD normal activity regarding the onset of jaundice and bilirubin levels which could be related to the timing of the oxidative stress exposure in their population relative to ours[20].

The two study groups characteristics were not homogenous. Approximately two-thirds of the G6PD normal activity group were Bahrainis, while 100% of the G6PD reduced activity group were Bahrainis. G6PD reduced activity is very common among Bahrainis; approximately 28% of Bahraini newborns are affected by G6PD reduced activity[21,22]. Nevertheless, this significant difference in nationalities may have affected the results. In addition, the sex ratio was significantly different in both study groups. The majority of the G6PD reduced activity group were males. G6PD reduced activity is an X-linked disorder that commonly affects males more than females. There was no significant difference in the feeding pattern in both groups.

CONCLUSION

A bilirubin level of 6mg/dl during the first neonatal day could be an indicator for the presence of G6PD reduced activity in a newborn. The relatively higher bilirubin level during the first day of life in G6PD reduced activity newborns could be a reflection of a prenatal or natal stress exposure that results in the early rise in serum bilirubin. Further prospective multicenter study is advised.

Author Contribution: All authors share equal effort contribution towards (1) substantial contribution to conception and design, acquisition, analysis and interpretation of data; (2) drafting the article and revising it critically for important intellectual content; and (3) final approval of manuscript version to be published. Yes.

Potential Conflicts of Interest: None.

Competing Interest: None.

Sponsorship: Arabian Gulf University, Bahrain.

Submission Date: 21 June 2016.

Acceptance Date: 4 July 2016.

Ethical Approval: Approved by the Ethical Committee, Arabian Gulf University and the Ministry of Health, Bahrain.

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