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Reference Values of Biochemical Parameters in Serum of Yemeni Children with Down Syndrome

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Abstract

Background: Biochemical tests are essential in the diagnosis and monitoring of diseases and requiring optimal reference range for accurate interpretation of laboratory tests. Genetic and phenotypic variability in Down syndrome is likely to impact the reference values of laboratory tests.
Aim: The aim of this study was to establish biochemical reference ranges for Yemeni children with Down syndrome.
Methods: This study was cross-sectional study carried out on 130 Yemeni children with Down syndrome (65 male and 65 female), aged 2 - 18 years, selected mainly from special needs centers for Down's syndrome in Sana'a city, Yemen, during 2019. Reference values for 10 biochemistry parameters were determined for Yemeni children with Down syndrome.
Results: All reference values of 10 biochemical tests fall within the existing reference range except for uric acid and phosphate had high reference values (2.2 – 7.4 mg/dl and 3.0 – 7.0 mg/dl, respectively). All the analyzed parameters showed non-significant differences between males and females except for uric acid and calcium reference values. Uric acid was significantly higher in males than females (2.3 – 7.9 mg/dl for males vs. 2.3 – 6.7 mg/dl for females, $P = 0.036$), and calcium reference values was significantly higher in males than females (8.3 – 10.3 mg/dl for males vs. 8.2 – 9.5 mg/dl for females, $P = 0.036$).
Conclusion: Established reference values for biochemical tests for Yemeni children with Down syndrome is important because it will help in the interpretation of laboratory results correctly.

Keywords: Reference Values, Down Syndrome, Yemeni Children, Biochemical Tests

1. Introduction

Biochemical tests are routinely prescribed in healthcare systems, and essential in the diagnosis and monitoring of disease, and required optimal reference range for accurate interpretation of laboratory tests, because factors such as genetics, altitude, environmental factors, and gender can affect laboratory tests [1-3].

Down syndrome, or trisomy 21, is a complex metabolic and genetic disorder that arises from the failure of segregation of chromosome 21 during meiosis of gametes, there are several reports on the increased incidence of Down syndrome, from different parts of the world, with respect to ethnicity and maternal age [4-11]. The overall incidence of Down syndrome worldwide for all age groups is 1/800 live births, and is shown to increase drastically to 1/400 in older mothers, those above 35 years of age, to as high as 1/12 by the age of 50 [4-7]. The presence of an extra chromosome 21 in Down syndrome results in overexpression of genes residing on that chromosome, which lead to gene dose effect that is thought to account for most of the pathophysiology changes of Down syndrome [12]. From a medical point of view, it is important to establish these changes in some laboratory parameters, because they should be differentiated from

those derived from disease and dose of genetics, also there are scarce in literature about reference values for Down syndrome individuals, so the aim of this study was to establish biochemical reference values for Yemeni children with Down syndrome to compare them with laboratory established or published reference ranges existing for the general population.

2. Methods

The present study was cross-sectional study, carried out on 130 Yemeni children with Down syndrome (65 male and 65 female), aged 2 - 18 years, selected mainly from special needs Centers for Down's Syndrome in Sana'a city, Yemen during 2019. The minimum sample size required for estimation of the reference values (2.5 and 97.5 percentiles) is 120 to obtain reliable estimates [13-14]. This study was approved by the Committee of Postgraduate Studies and Scientific Research of the Faculty of Medicine and Health Science, Sana'a University. Written informed consent was obtained from parents of participants prior to involving them in the study.

Venous blood (6 ml) was collected from each participant into labeled plain test tubes for determination of total protein, albumin, total bilirubin, blood sugar, calcium, phosphate, urea, creatinine, uric acid and glutamic pyruvic transaminase (GPT) by Cobas Integra 400 plus auto-analyzer (Roche, Germany).

The results were analyzed by Social Package of Statistical Science (SPSS) version 21 (LEAD Technologies; Inc. USA). The reference values include 95% of the test results and bounded by the 2.5 and 97.5 percentiles. In normally distributed data, the 2.5th and 97.5th percentiles were determined parametrically, but in non-normally distributed data, the 2.5th and 97.5th percentiles were determined non-parametrically. Kolmogorov-Smirnov Test was performed to distinguish between parametric and non-parametric data, if the results of the Kolmogorov-Smirnov test with p-value > 0.05, the data is normally distributed (parametric data), and if p-value <0.05, the data is not normally distributed (non-parametric data). Differences in variables between male and female that were normally distributed were tested using Independent sample T-test, while differences in variables that were not normally distributed were tested using Mann-Whitney test.

3. Results

This study included 130 participants with a mean age of 9.6 ± 3.8 years and a mean body mass index (BMI) of 17.8 ± 4.7 kg/m^2. The mean ± SD and 95% reference values (2.5th – 97.5th percentiles) for biochemical tests for parametric data are shown in Table 1. All measurements fall within the existing reference range except for uric acid had high reference values. It is observed that all the analysed parameters show non-significant differences between males and females except for uric acid reference values that was significantly higher in males than females (2.3 - 7.9 mg/dl for males vs. 2.3 - 6.7 mg/dl for females, *P* = 0.036).

Table 1: Biochemical tests reference values for parametric data in Yemeni children with Down syndrome

Analyte (unit)	Sex	No	Mean ± SD	Percentile 2.5th	Percentile 97.5th	Reference values	*P* value
Random blood sugar (mg/dl)	Males	65	95±19	57	133	57-133	0.469
	Females	65	98 ±17	64	132	64-132	
	Total	130	96 ±18	60	132	60-132	
Uric acid (mg/dl)	Males	65	5.1±1.4	2.3	7.9	2.3-7.9	0.036
	Females	65	4.5±1.1	2.3	6.7	2.3-6.7	
	Total	130	4.8±1.3	2.2	7.4	2.2-7.4	
Protein (g/dl)	Males	65	7.0±0.5	6.0	8.0	6.0-8.0	0.827
	Females	65	7.0±0.54	5.9	8.1	5.9-8.1	
	Total	130	7.0±0.5	6.0	8.0	6.0-8.0	
Total bilirubin (mg/dl)	Males	65	0.56±0.07	0.42	0.70	0.42-0.70	0.938
	Females	65	0.56±0.09	0.38	0.74	0.38-0.74	
	Total	130	0.56±0.08	0.4	0.72	0.4-0.72	

The median (range) and 95% reference values (2.5th – 97.5th percentiles) for biochemical tests for non-parametric data are shown in table 2. All measurements fall within the existing reference range except for phosphate had high reference values. It is observed that all the analyzed parameters show non-significant differences between males and females except for calcium reference values that was significantly higher in males than females (8.3 - 10.3 mg/dl for males vs. 8.2 - 9.5 mg/dl for females, *P* = 0.036).

Table 2: Biochemical tests reference values for non-parametric data in Yemeni children with Down syndrome

Analyte (unit)	Sex	No	Median (range)	Percentile		Reference values	*P* value
				2.5^{th}	97.5^{th}		
GPT (U/L)	Males	65	14 (5-30)	5	29.7	5-29.7	0.060
	Females	65	13 (5-25)	5	24	5-24	
	Total	130	13 (5-30)	5	27	5-27	
Creatinine (mg/dl)	Males	65	0.55 (0.35-0.8)	0.35	0.8	0.35-0.8	0.751
	Females	65	0.56 (0.3-0.8)	0.3	0.78	0.3-0.78	
	Total	130	0.56 (0.3-0.8)	0.3	0.8	0.3-0.8	
Urea (mg/dl)	Males	65	16 (10-35)	10	34.6	10-34.6	0.160
	Females	65	15 (10-33)	10	32	10-30.7	
	Total	130	15.5 (10-35)	10	33	10-33	
Albumin (g/dl)	Males	65	4.5 (3.2-5.3)	3.2	5.2	3.2-5.2	0.254
	Females	65	4.4 (3.3-5.3)	3.3	5.2	3.3-5.2	
	Total	130	4.4 (3.2-5.3)	3.2	5.2	3.2-5.2	
Calcium (mg/dl)	Males	65	9.1 (8.3-10.5)	8.3	10.3	8.3-10.3	< 0.001
	Females	65	8.6 (8.2-9.6)	8.2	9.5	8.2-9.5	
	Total	130	8.9 (8.2-10.5)	8.2	10	8.2-10	
Phosphate (mg/dl)	Males	65	5.5 (3.0-7.1)	3.0	7.0	3.0-7.0	0.140
	Females	65	5.1 (3.0-7.7)	3.0	7.6	3.0-7.6	
	Total	130	5.4 (3.0-7.7)	3.0	7.0	3.0-7.0	

4. Discussion

Biochemical tests are essential in the diagnosis and monitoring of diseases and requiring optimal reference range for accurate interpretation of laboratory tests, so this study represent a useful preliminary step in determining whether to develop separate reference range for Yemeni children with Down syndrome because genetics induces a variety of physiological and laboratorial changes. The results obtained from Yemeni children with Down syndrome demonstrated that uric acid and phosphate reference values are higher than laboratory established or published reference ranges existing for the general population. The higher levels of uric acid and phosphate may be attributed to the fact that, a number of genes located on chromosome 21 encode enzymes that are thought to be involved in numerous metabolic pathways such as inositol, energy, cholesterol, choline, purine and reactive oxygen species pathways [15]. For example, adenosine deaminase, one of the enzymes in purine catabolism, shows increased activity in the erythrocytes of Down's syndrome individuals [16], and this may be associated with increased purine catabolism in these individuals that lead to increase uric acid production. On the other hand, the activity of glucose-6-phosphate dehydrogenase has been reported to be increased in the erythrocytes and leucocytes of Down's syndrome individuals [17], which may lead to purine over-production and increase uric acid production. The increase of uric acid in this study was in agreement with previous studies [18-19].

5. Conclusion

Established reference values for biochemical tests for Yemeni children with Down syndrome is important because it will help in the interpretation of laboratory results correctly.

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Competing interests
The authors declare that they have no competing interests.

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