SHORT COMMUNICATION

Lower Plasma Soluble Transferrin Receptor Range in Healthy Indian Pediatric Cohort as Compared to Asian and Western Data

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Abstract Soluble serum transferrin receptor is derived from erythroid transferrin receptor expressed on surface of developing erythroid cells. It can be detected in blood using sensitive ELISA methodology and blood levels reflect physiological iron dependent erythropoiesis state in bone marrow. Normal adult levels vary from 2 to 5 mg/l. However, pediatric studies are few and describe normal ranges to the tune of 1.0–3.0 mg/l, which are relatively lower than that of adults. In present study 40 healthy children (2–12 years) were evaluated to establish normal soluble transferrin receptor range. The mean transferrin receptor levels were 0.39 mg/l with a range of 0.17–2.1 mg/l. The levels were low as compared to mean levels described in other studies from West and our country (4.39 and 2.0 mg/l respectively). Since, no internationally standard method for reporting and testing for transferrin receptor levels are yet available, hence it is imperative to establish normal control ranges in different population cohorts, especially in pediatric age group, to better interpret their levels in diagnostic context.

Keywords Asian · Controls · Pediatric · Soluble transferrin receptor · Western

Soluble plasma transferrin receptor is primarily derived from developing red blood cells in marrow. The truncated surface receptor released into blood reflects physiological iron dependent erythropoiesis state in bone marrow. Hence,

levels are increased in states of iron deficiency and reduced in cases of marrow failure or aplasia [1]. Unlike plasma ferritin levels, which are influenced by inflammation and underlying cytokinemia, soluble transferrin receptor levels remain largely unaffected. Hence, they are used as a marker to diagnose iron deficiency state especially in cases with added inflammation [2]. Rather many studies have shown that plasma transferrin receptor to log ferritin ratio is a better indicator of iron deficiency with levels >1.5 suggestive of iron deficiency and <1.5 anemia of chronic disease [3, 4].

However, before the plasma transferrin receptor levels can be interpreted in clinical context normal population ranges need to be established, since there are no internationally available standards as well as standardized reporting methodology. Normal adult male and female levels in various studies have been found to range from 2.2 to 5.0 and 1.9 to 4.4 mg/l respectively [5, 6]. Pediatric studies are few and most highlight relatively lower soluble transferrin receptor levels as compared to normal adults [7–10]. In present pilot study, we evaluated plasma soluble transferrin receptor levels in 40 healthy children (2–12 years) over a period of 6 months. Two ml of blood sample in EDTA was collected after written informed consent and was run same day on fully automated blood cell counter (Beckmann coulter HMX 500) for complete blood count and for serum ferritin by ELISA (Orgentec, Germany). Plasma samples of controls with normal hemoglobin levels for age and gender and normal RBC indices and ferritin values (>12 µg/l) were then stored at –20 °C for batch analysis for soluble transferrin receptor levels. Plasma soluble transferrin receptor level assay was performed by sandwich ELISA methodology as per manufacturer's insert in the kit (Qayee-Bio, Shanghai, China).

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Out of 40 subjects enrolled, 23 (57.5 %) were boys and 17/40 (42.5 %) girls. The age ranged from 2 to 12 years with a mean of 9 years. The Hb ranged from 11 to 14 gm/dl with mean Hb of 12 gm/dl. The RBC indices and RDW (red cell distribution width) were within normal range for all cases. The plasma ferritin levels ranged from 13 to 171 µg/l with a mean $\pm$ SD of 31.21 ± 17.12 µg/l. The soluble transferrin receptor levels in the control cohort ranged from 0.17 to 2.1 mg/l with a mean $\pm$ SD of 0.39 ± 0.41 mg/l and a median of 0.23 mg/l (see Fig. 1). In boys the soluble transferrin receptor levels ranged from 0.19 to 2.1 mg/l with a mean $\pm$ SD of 0.44 ± 0.50 mg/l as compared to 0.17–0.98 mg/l with a mean $\pm$ SD of 0.33 ± 0.23 mg/l in girls (see Fig. 2). On *t* test comparison, the difference was not statistically significant ($p = 0.36$) between the gender groups.

As already stated above, pediatric ranges for soluble transferrin receptor are low as compared to levels in healthy adult males/females. The current pilot study too had low ranges in healthy pediatric subjects when compared with reference ranges described in adults. In addition, levels were found to be even lower than those described in pediatric age group in various western studies. In a large cohort of 268 healthy children, Ooi et al. [7], noted the range for soluble transferrin receptor in 2–12 years age group as 0.81–2.91 mg/l with a mean $\pm$ SD of 1.58 ± 0.37 mg/l. In another large study cohort of 301 healthy children, Suomenin et al. [8] highlighted progressive regression of normal range of soluble transferrin receptor in children aged 6 months–16 years. Their study found ranges as 1.5–3.3, 1.3–3.0 and 1.1–2.7 mg/l in children aged 6 months–4 years, 4–10 years and 10–16 years respectively. Antilla et al. [11] and Choi et al. [12] also highlighted in their studies that soluble transferrin receptor ranges decrease with age from infants to adolescence age group. Tong et al. [13] in a study involving 110 infants found soluble transferrin receptor levels comparable to that of adults with a mean of

Fig. 1 Distribution of soluble transferrin receptor level (mg/l) data in control subjects

Fig. 2 Bar chart showing soluble transferrin receptor ranges (min, max and med) in boys and girl

4.39 ± 1.70 mg/l. In studies from our subcontinent, Aslam et al. [9] from Pakistan, noted the range for soluble transferrin receptor in children 2–11 years to be 1–2.9 mg/l with a mean of 1.95 mg/l in girls and 2.0 mg/l in boys. Goyal et al. [10] in their study involving 25 healthy pediatric subjects, found soluble transferrin receptor range to be 0.3–2.9 mg/l with a mean of 2.0 mg/l. It is interesting to note the lower ranges in our healthy children cohort and suggests large community/population based studies to better define reference ranges for soluble transferrin receptor, before the same can be utilized as a marker for early iron deficiency in anemia of chronic disease cases in clinical practice.

Compliance with Ethical Standards

Conflict of interest There is no conflict of interest.

Ethical Standards All procedures performed in studies involving human participants were in accordance with the ethical standards of the institutional and/or national research committee and with the 1964 Helsinki declaration and its later amendments or comparable ethical standards. Around 2 ml of blood sample in EDTA was drawn under aseptic precaution after obtaining informed written consent from all control healthy children/guardians or parents. The study was duly approved by the Institutes Ethics committee.

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