Biotinidase deficiency (BD) is a biotin responsive, autosomal recessive inherited neurocutaneous, treatable metabolic disorder. It occurs due to the deficiency of an enzyme biotinidase, which is involved in biotin cycle. As a result of BD the vitamin biotin is not recycled in biotin cycle. The deficiency of biotinidase can be partial or profound based on the level of activity of biotinidase enzyme; it is considered as partial BD when biotinidase activity is 10-30% of mean normal serum enzyme activity and profound BD when it is less than 10% mean serum enzyme activity.

Untreated individuals with profound BD usually manifest neurological and cutaneous features mostly between second and fifth month of life. However, some patients can present in late adolescent or even in adult life. Neurological manifestations include hypotonia, developmental delay, ataxia, sensorineural hearing impairment, optic atrophy and seizures. Seizures can be tonic-clonic, myoclonic, partial, or infantile spasms and are often resistant to anti-convulsant medicines. Cutaneous manifestations of BD include atopic or seborrhic dermatitis, partial or complete alopecia and fungal skin infections. Some individuals with untreated BD develop metabolic decompensation resulting into severe metabolic acidosis, lactic acidosis, ketosis and hyperammonemia, which can progress to coma and death. Most of these patients report to general paediatricians but they may seek specialist care from neurology, dermatology or ophthalmology; if symptoms are limited to these systems. Almost all symptoms respond dramatically to oral biotin expect optic atrophy, sensorineural hearing impairment and development delay, which is usually irreversible.

Global incidence of BD is 1 in 60,000 live births. Even higher incidence is reported from countries like Turkey and Saudi Arab where there is high rates of consanguinity. In Pakistan incidence of BD is unknown. There are no cases reported from Pakistan however a number of Pakistani children living in other countries are reported to have BD. This signifies that BD is very much present in our country but patients are not recognized and diagnosed locally due to lack of awareness of the condition among physicians and absence of local diagnostic facility. Biotinidase activity is reliably measured in serum and plasma using either semiquantitative fluorometric method using biotin 6-amidoquinoline as substrate or semiquantitative colorimetric method using N-biotinyl-p-aminobenzoic acid as substrate but is unfortunately currently not available in Pakistan.

Sometimes BD is clinically suspected by physicians but their inability to make definite diagnosis due to unavailability of diagnostic test in Pakistan leads to numerous long-term consequences. As neither the physician nor the patient is confident of the diagnosis, importance of compliance to life-long treatment with oral biotin is neither emphasized by the physician nor its significance completely appreciated by the patient. This leads to erratic compliance resulting into recurrence of symptoms within weeks to months of stopping oral biotin contributing to both morbidity and mortality. Treatment with inadequate dose of oral biotin is also a commonly observed issue. Recommended dose of oral biotin for children with BD is 5-20mg of biotin per day independent of age and weight. Biotin tablets mostly available locally are of 600microgram strength. Patients require 10-40 tablets per day of this current (600 mcg) formulation. Patients are often prescribed 1 tablet (600microgram) two or three times a day. Such inadequate dose doesn't result in amelioration of symptoms, which at many a times results into loss of faith upon physicians clinical competence among patients and their care takers.

Biotinidase deficiency has an inexpensive and reliable screening test, it is easily treatable and has a high morbidity and mortality in untreated cases. Therefore it is included in national newborn screening programmes of all states of United States and thirty other countries. There is known significant intra-familial variation both in the spectrum as well as the age of onset of BD. In the absence of national newborn screening programme in Pakistan, physicians in Pakistan must screen all first-degree relatives of individuals with BD for BD and treated if they are found to be affected.

Biotinidase deficiency is considered as one of the most rewarding metabolic disorders to treat. Health care providers need to be aware of the condition and should make efforts to make definite diagnosis by getting biotinidase activity estimation from overseas labs in order to ensure prompt treatment, good compliance and proper counseling for the need of life-long treatment. Biotinidase activity estimation can be easily sent to overseas labs by collecting dried blood spots on filter papers and sending through regular postal services. However, the need for locally available facility for biotinidase assay cannot be emphasized enough. All leading institutes of Pakistan should look into the feasibility of biotinidase activity
estimation testing, so that it is easily available locally. Ministry of health or National Institute of Health should arrange for biotinidase testing in Pakistan. Physician’s awareness is the most important step to properly identify and treat these patients. Identification of a case must be followed by family screening for early identification of cases. All affected individuals need periodic life-long follow-ups including hearing and visual assessments.

References