ESTIMATION OF REFERENCE VALUES IN LIVER FUNCTION TEST IN HEALTH PLAN INDIVIDUALS OF AN URBAN SOUTH INDIAN POPULATION

Sultana Furruqh, D. Anitha and T. Venkatesh

Department of Clinical Biochemistry, St. John’s Medical College Hospital, Bangalore - 560 034, INDIA

ABSTRACT

Reference intervals in clinical chemistry are commonly based on results of measurements in reference western population or are taken from the western literature. Reference Values are thought to aid physicians to interpret results of measurements and should be representative of a defined group of individuals. This group should be as similar as possible to the patients under investigation. The reference population in this study has been recruited from the individuals attending the Health Plan Clinic who fulfill the defined inclusion and exclusion criteria as well as defined partition criteria. The samples were sorted based on the decision by the physician. The emerging group of individuals was considered as a reference population for the hospital patients and the results of measurements in this study was evaluated statistically to stress on the urgent need to establish the in-house reference values. The reference limits are defined as the central 95 percentile of the population after eliminating the outliers. The lower reference limit is the 2.5 percentile while the upper reference limit constituted the 97.5 percentile for the population.

KEY WORDS

Reference Intervals, Age, Gender, Reference Population.

ABBREVIATIONS

AST, Aspartate Aminotransferase; ALT, Alanine Aminotransferase; ALP, Alkaline Phosphatase; \( \gamma \)-GT, Gamma - Glutamyl Transferase.

INTRODUCTION

A major need for laboratory medicine and clinical chemistry personnel in particular, is to provide the clinicians updated & appropriate information in Reference Values, previously known as normal values. Introduction of the concept of Reference Values and Reference population simplifies the task for laboratories; as long as they define the reference population, the outcome can always be recognized as Reference Values and Reference Intervals. Selecting Reference individuals is an essential but difficult step in the production of Reference Values throughout the world (1) (Fig 1).

Author for correspondence:

Dr. Sultana Furruqh,
Professor and Lab In-charge,
Department of Clinical Biochemistry,
St. John’s Medical College Hospital,
Bangalore - 560034, INDIA
E-mail: sfurruqh@yahoo.com

There have been many attempts to create reference Intervals without going through the laborious methods originally described by Grasbeck and Alstrom (2) or in the IFCC recommendation (3). Harris and Boyd (4) have comprehensively discussed the theory of Reference Values from a bio-statistical viewpoint. In recent years' Nano et al. (5), have shown considerable usefulness of defining Reference Intervals for a few quantities from carefully selected hospitalized patients.

So far there is, no established large population based study, on reference limits in Indian population. The reference limits in use are either borrowed from the textbooks and articles or insert literature from the kit manufacturers. The upper and lower limit of measurements varies dependent on source of information as well as the methodology followed. There is a need to realize, whether, there is a requirement for restructuring the reference interval for an Indian population. The aim of the current study was conducted based on
Fig. 1. Standard terminology for the description and discussion of reference values

<table>
<thead>
<tr>
<th>Reference individuals</th>
<th>Reference population</th>
<th>Reference sample group</th>
<th>Reference values</th>
<th>Reference distribution</th>
<th>Reference limits</th>
<th>Reference intervals</th>
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<tbody>
<tr>
<td>Comprise a</td>
<td>From which is selected a</td>
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<td>From which are calculated</td>
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these needs so that parameters evaluated in the healthy defined group of individuals would serve as the Reference Values for the Reference population.

MATERIALS AND METHODS

This retrospective study was conducted in the Department of Clinical Biochemistry at St. John’s Medical College Hospital for a period of 4 years (1999 to 2002). The sampling strategy used was the posteriori sampling. In the posteriori sampling, a direct method which uses a database containing both analysis results and information on a large number of individuals. Values of individuals fulfilling defined inclusion criteria are selected. The individuals were selected from the population attending the Health Plan Clinic, which is a preventive medical center, a part of St. John’s Medical College Hospital. In the Health Plan clinic, all individuals are evaluated by a physician and for most of the biochemical parameters. Individuals opting for Executive Health Check up are evaluated in detail by a physician and a consultant as per the individual preferences. The biochemical evaluation is also done to assess liver and renal function, lipid profile and glucose levels. Amongst 2500 individuals attending the clinic, 1500 individuals had opted for executive health check up. Remaining 1000 individuals were eliminated because they opted for health check up, which was not accompanied by the above-mentioned evaluation with the physician. Out of the 1500 selected subjects, 664 individuals belonging to the age group between 20 to 70 years were selected for the study after excluding the subjects as per the criteria (6) given in the table no.1. Among the 664 individuals, 464 individuals were men and the remaining 200 individuals were women.

The blood specimens were drawn from the individuals in the morning between 8:30 AM and 9:30 AM. Vacutainers (Becton Dickinson) with clot activator specific for serum were used for the collection of venous blood sample. All the samples were drawn after an overnight fast. This is the regular protocol followed in the hospital for the individuals attending the Health Plan Clinic.

In the study group, defined by gender and age, the first step was to eliminate all results, which were marked lipemic, hemolytic or icteric. Then the median and central 98 percentiles were calculated and results outside these limits eliminated before the final median and central 95 percentile was calculated. The 97.5 percentile and 2.5 percentile formed the upper and lower reference limits of the population. A summary of the results is given in Table 2 and 3 together with the reference intervals in use at the laboratory.

Measurement Procedures

To ensure the reproducibility and repeatability of the test results, the laboratory participated in established external quality assessment programs (BIORAD) and had a comprehensive internal quality control program and results were accordingly released. The Quality control check was done every day and SD, percentage of coefficient of variation (CV) was calculated (Table 4). Liver Function Parameters in serum were analysed using Dade Dimensions (Dade RxL). Statistical analysis was done using SPSS package. The median and central 98 percentiles were calculated and results outside these limits eliminated before the final median and central 95 percentile was calculated. Liver function parameters were estimated using IFCC approved method. Total Protein and Serum Albumin were estimated using Biuret (7, 8) and Bromocresol Green method (9, 10). Albumin to