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Hematological and Biochemical Reference Intervals in Nepal: A Narrative Review

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ABSTRACT

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An accurate interpretation of hematological and biochemical parameters is important for clinical diagnosis and decision making. Hematological parameters, such as hemoglobin, hematocrit, and white blood cell counts, tell about blood health, while biochemical parameters, including liver enzymes, renal markers, lipid profiles, and blood glucose, indicate metabolic and organ function.

Reference Intervals (RI), which statistically represent central 95% values of healthy individuals, vary by population due to different factors. This narrative review aims to evaluate the hematological and biochemical reference ranges currently used in major hospitals across Nepal. In this review laboratory reference intervals for regular hematological and biochemical parameters used in 8 different hospitals from Nepal, which are located in Provinces 2, 3 and 4, with internationally accepted standard intervals, taken from recognized international guidelines, including World Health Organization and American Diabetes Association and comparison was done.

Laboratory data were collected using a preset proforma designed to systematically record reference ranges from blank report sheets of the respective hospitals. It was found that most of the reference intervals used by these hospitals slightly varied with the internationally accepted standard intervals. However, some parameters like Fasting Blood Sugar, Blood Urea, and CT showed larger variations. Therefore, for accurate diagnosis and treatment of patients in Nepal, such a range of reference intervals shall be used that are based on the country's population, diet, genetics and environment. It is also essential to update the intervals on a timely basis. This ensures the most effective decisions which doctors can make for a patient's health.

Keywords: Biochemical; hematology; laboratory; reference intervals.

INTRODUCTION

Laboratory medicine plays a key role in diagnosis, prognosis, patient management, and preventive healthcare. Laboratory reference intervals are crucial for interpreting test results, but locally established intervals are limited in Nepal.

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A study in the Kaski District in year 2022 established dry-chemistry based reference intervals for urea, creatinine, sodium and potassium in healthy adults and found significant differences from manufacturer-provided or foreign-based ranges.[1] Additionally, another nationwide study involving 617 healthy Nepalese adults derived reference intervals for 30 biochemical analyses and noted that values for parameters such as urea, ALT, cholesterol and triglycerides differed from international data.[2] These findings underscore the importance of systematic efforts to produce population-specific hematological and biochemical reference intervals that reflect Nepal's unique genetic, environmental, altitude and dietary variations, thus promoting improved laboratory accuracy and patient care.

In this review, laboratory investigation forms were collected from Hetauda Hospital, Shahid Dharmabhakta National Transplant Centre, Provincial Hospital Sarlahi, Tribhuvan University Teaching Hospital, Bir Hospital, Patan Hospital, Teku Hospital, and Gandaki Medical College, following

appropriate permissions. There was no involvement of patient directly or indirectly. Internationally accepted reference intervals were obtained from recognized guidelines, including those of the World Health Organization (WHO)[3] and the American Diabetes Association (ADA)[4] and a comparative analysis was conducted.

REFERENCE INTERVAL

Reference Interval (RI) is simply define as the prediction interval which includes the central 95% of reference values (RVs), or test results from well-defined healthy individuals (reference individuals).[5] It represents a parameter's range between upper and lower limit values that are used in a lab test. The values for an individual are affected by several factors like age, sex, blood type; biological samples like urine, spinal fluid; and situational conditions like fasting and physical activities.[6] In the past, laboratories used self-established ranges named 'normal range'. However, this was criticized later as the reference intervals for healthy individuals vary across regions, and establishing a normal range using a small defined sample of people would not prove effective for other people from different regions.[7,8,9]

Normal ranges would have led to confusion for accurate comprehension, establishing emotional distress among patients. Therefore, statistically accurate intervals specific to a demographic region were necessary that would accurately interpret the lab report of individuals, thus leading to establishment of 'reference intervals'.[10] Reference intervals are of two main types: health-associated reference intervals, derived from individuals in good health, and decision-based reference intervals, which define medical decision limits used by clinicians for diagnosis and patient management.[11,12] Reference intervals vary between countries because they are influenced by ethnicity, genetics, diet, environment, lifestyle and analytical methods; thus locally established intervals are essential for accurate interpretation.[13]

HEMATOLOGICAL PARAMETERS

Hematological parameters refer to the measurable components and characteristics of blood, which can include factors such as cell counts, hemoglobin levels, and other indicators that reflect the physiological status of an organism. Changes in these parameters can indicate biological dysfunction and are influenced by external stimuli and the presence of xenobiotics.[14] The following are hematological parameters included in this study: Hemoglobin (Hb), Red Blood Cell (RBC) count, Platelets, Total Leukocyte Count (TLC), Neutrophil, Lymphocyte, Monocyte, Eosinophil, Basophil, ESR, Bleeding Time (BT), Clotting Time (CT), and Prothrombin Time (PT). The data for Hematological standard values included in the table consists of internationally accepted standard ranges, taken from WHO and other sources.[15,16,17,18]

BIOCHEMICAL PARAMETERS

Blood biochemical parameters refer to the various measurable components and characteristics of blood plasma or serum, including fractions of proteins and lipids, which are essential for evaluating animal health, diagnosing diseases, and assessing biological functions.[19]

The following are the biochemical parameters included in this study: Blood Sugar F, Blood Sugar PP, Blood Urea, Serum Creatine, Sodium (Na+), Potassium (K+), Serum Uric Acid, Serum Albumin, Serum Protein, Serum Calcium, and Serum Amylase. Similarly, the data for Biochemical standard values included in the table consists of internationally accepted standard ranges, taken from WHO and other sources.[20-25]

REAGENT AND SOFTWARE USED

The determination of reference intervals in experimental investigations is highly dependent on the reagents used. In clinical laboratory testing, the use of high-quality reagents is critical, as different reagents can yield varying results. Consistency in reagent selection throughout the testing process is essential to avoid misinterpretation of results. Moreover, when transferring a reference interval, it is important to ensure that the reagents used are compatible with those employed in the original determination.[26,27] To ensure comparability of medical test results, it is crucial to standardize all aspects of the measurement process, including minimizing variation introduced by different machines or analytical instruments. Traceability to higher-order reference standards can be achieved through the use of reference measurement systems, ensuring accuracy and consistency across laboratories.[28]

INTERHOSPITAL COMPARSION OF HEMATOLOGICAL AND BIOCHEMICAL PARAMETERS IN NEPAL

In haematology, parameters such as hemoglobin, RBC count, and platelet count generally remain within standard ranges, though slight differences are observed in lower and upper limits; for example, hemoglobin lower limits range from 11 g/dL (Hetauda, Patan, Gandaki) to 13.5 g/dL (TU Teaching), and RBC counts show broader ranges in some hospitals (Hetauda: 4.0-6.5 million/cumm). Total Leukocyte count of 4000-11000 million/cumm is a common interval used by many

of the included hospitals that aligns with the international standards. However, Gandaki Medical college uses smaller intervals with 4000-10000 million/cumm and Shahid Dharmabhakta National Transplant Centre includes a range for newborn babies whose upper limit extends up to 15000 million/cumm. Neutrophil ranges mostly align with international standards with many intervals starting from 40% or 45% till 70% or 75%. A notable monocyte difference can be seen in Gandaki Medical College as the intervals used here is 3%-12%, whereas the standard intervals are 2%-8%. The largest variation in Clotting Time (CT) is seen in Bir Hospital and Patan, where for Bir Hospital it ranges from 5–10 minutes, and Patan from 6-15 minutes. PT ranges from 10-13 seconds (standard) to 12-16 seconds (Gandaki Medical College), which could impact anticoagulation therapy monitoring.

Significant differences exist between reference ranges used in Nepali hospitals and internationally accepted biochemical standards. For example, Fasting Blood Sugar (FBS) is 60–120 mg/dL in most Nepali hospitals versus <100 mg/dL internationally. Electrolyte levels also vary: Sodium (Na^+) lower limits are 124 mmol/L in Provincial Hospital Sarlahi compared to 135 mmol/L internationally, while Potassium (K^+) ranges differ slightly (3.0–5.5 mmol/L vs. 3.5–5.0 mmol/L), which may be critical for cardiac patients. Serum Uric Acid standards abroad are gender-specific (males: 3.4–7.0; females: 2.4–6.0 mg/dL), but several Nepali hospitals apply a single range (2.0–7.0 mg/dL), risking under-detection of hyperuricemia in males. Similarly, Serum Amylase upper limits vary widely from <80 U/L (Bir, Teku) to 180 U/L (Sarlahi) potentially affecting pancreatitis diagnosis. (Table 1)

However the inter-hospital differences in reference range observed in our study are more likely due to the use of different analytical platforms, reagent kits, and calibration protocols from various manufacturers that provide their own reference intervals. Since most laboratories in Nepal adopt reference ranges that manufacturer provides rather than calculating population-based intervals, these variations do not necessarily reflect true demographic, genetic, or nutritional differences. This emphasizes the urgent need for Nepal-specific population-derived reference intervals.

Table 1: Inter-hospital comparison of Hematological and Biochemical Parameters in Nepal

Investigations	Standard Ranges	Hetauda Hospital	Shahid Dharmabhakta National Transplant Center	Provincial Hospital Sarlahi	TU Teaching Hospital	Bir Hospital	Patan Hospital	Teku Hospital	Gandaki Medical College
		Province 3		Province 2		Province 3			Province 4
Haematology									
Hb (g/dL)	Male: 14-18, Female: 12-16	(11-18)	Male (13-18), female (11-16)	Female: 11-16, Male: 12-18	13.5-18.0	12.0-16.0	11.5-15.0	12.0 - 18.0	11.0-16.0
RBC(million/cumm)	Males: (4.7-6.1), Females:(4.2-5.4)	(4.0-6.5)	Male: 4.5-5.5, female: 3.8-4.8	3.5-5.5	4.5-5.5	4-5.5	4.0-5.5	4.2-5.9(male), 3.8-5.2(female)	4.0-5.9
Platelets	(1.5-4.0) Lakh/cumm	(1.5-4.0) Lakh/cumm	1.5-4.0 lakh/cumm	1.5-4.0 lakh/cumm	1.5-4.5 lakh/cumm	1.5-4.0 lakh/cumm	1.5-4.0 lakh/cumm	1.5-4.5 lakh/cumm	1.5.4.5 lakh/cumm
Total Leucocyte Count(/cumm)	(4000-11000)	(4000-11000)	Adults: 4000-11000, Newborn: up to 15000	4000-11000	4000-11000	4000-11000	4000-11000	4500-11000	4000-10000
Differential count									
Neutrophil	45-75%	40-75%	40-70%	40-70%	45-75%	40-70%	40-65%	50-65%	50-70%
Lymphocyte	20-40%	20-40%	20-45%	20-45%	25-45%	20-45%	20-40%	20-40%	20-40%

Monocyte	2-8%	2-10%	2-6%	2-10%	2-10%	2-10%	2-8%	2-8%	3-12%
Eosinophil	1-4%	2-6%	0-4%	1-6%	1-6%	1-6%	1-5%	1-4%	0.5-5.0%
Basophil	0-2%	0-1%	0-2%	0-1%	0-1%	0-1%	0-1%	0-1%	0-1%
ESR (mm 1st hr)	Male:(0-15), Female: (0-20)	(0-20)	Male (0-9), Female: (0-20)	Male (0-9), Female (0-20)	0-15	0-20	0-15	Male: 0-15, Female: 0-20	0-20
BT(Bleeding Time)	2-7 minutes	2-6 minutes	IVY method: 2-7 minutes, Duke's: 2.5-9.5 minutes	1-6 minutes	1-7 minutes	2-7 minutes	2-6 minutes	2-7 minutes	1-6 minutes
CT(Clotting Time)	8-15 minutes	5-12 minutes	6-10 minutes	6-10 minutes	6-12 minutes	5-10 minutes	6-15 minutes	6-15 minutes	5-12 minutes
PT(Prothrombin Time)	10-13 seconds	10-14 seconds	11-16 seconds	12-15 seconds	11-15 seconds	10-15 seconds	11-16 seconds	11-13.5 seconds	12-16 seconds
Biochemistry									
Blood Sugar F (mg/dL)	<100/WHO and ADA	60-120	60-100	60-120	63-110	70-110	60-110	70-110	60-110
Blood Sugar PP (mg/dL)	<140/ WHO and ADA	60-140	60-140	Below 150	below 140	80-140	60-150	below 150	60-150
Blood Urea (mg/dL)	7-20	20-40	15-45	15-45	9-39	13-43	20-45	15-43	15-40
Serum Creatine (mg/dL)	Male: 0.7-1.3, Female: 0.6-1.1	0.4-1.3	0.4-1.4	0.9-1.2	0.68-1.36	0.4-1.4	0.6-1.3	0.4-1.4	0.6-1.5
Sodium (Na+) (mmol/L)	135-145	135-150	135-145	124-145	135-150	135-145	130-150	135-145	135-150
Potassium (K+) (mmol/L)	3.5-5.0	3.5-5.5	3.5-5.0	3.5-5.5	3.5-5.5	3.0-5.0	3.5-5.5	3.0-5.0	3.5-5.3
Serum Uric Acid (mg/dL)	Males: 3.4-7.0, Females: 2.4-6.0	2.0-7.0	Male: 4.0-7.0, Female: 2.4-5.7	2-7	2.5-7.4	Male: 2-7, Female: 2-6	2.4-7.0	2.0-7.0	4.0-6.0
Serum Albumin (gm/dL)	3.5-5.0	3.5-5.5	3.5-5.5	3.4-5	3.5-5.0	3.5-5.5	3.4-5.0	3.5-5.5	3.2-5.5
Serum Protein (gm/dL)	6.0-8.3	5.0-8.0	6.0-8.0	6-8	5.0-8.0	5.0-8.0	6.0-8.0	6.0-8.0	6.0-8.0
Serum Calcium (mg/dL)	8.5-10.5	8.0-11.0	8-11	8.2-10.2	8.5-11.0	8.0-11.0	8.5-10.5	8.0-11.0	8.0-10.5
Serum Amylase (U/L)	30-110	35-145	<120	60-180	<110	<80	<120	<80	<110

SUMMARY

This narrative review compares some hematological and biochemical RIs from various Nepali hospitals with internationally accepted standard intervals. It was found that many RIs used by these hospitals closely aligned with standard intervals, but greater variations

existed for parameters like Fasting Blood Sugar and Blood Urea that may be due to difference in demographics and methodologies. This review highlights that reference intervals currently used in Nepali hospitals vary considerably, mainly because of differences in analyzers and manufacturer-calibrated reference ranges utilized by laboratories. These findings add emphasis to the need for population-based research to establish Nepal-specific reference ranges. In the long term, analytical procedures will need to be harmonized and reagents be standardized among laboratories in order to improve inter-laboratory comparability and accuracy in diagnosis.

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