Research Article

A National e-Survey of Adult Reference Intervals of Routine Chemistry Analytes Used by Laboratories across Pakistan: A Step Towards Harmonization

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Abstract

Objectives: To identify the variation of reference intervals, reporting units used for key blood chemistry parameters in laboratories across Pakistan and to understand the factors contributing to these discrepancies.

Methodology: A comprehensive e-questionnaire developed using google forms covering key blood chemistry parameters (Electrolytes, fasting glucose, glucose random urea, creatinine and lipid profile), reference intervals, reporting units, and laboratory practices was administered via email to the Pathologists. Frequency and percentages were calculated for each response and descriptive results were also evaluated.

Result: A total of 38 responses were received five responses were excluded due to incomplete forms. The responses from 33 laboratories revealed substantial variability in reference intervals (RIs) for routine blood chemistry parameters, underscoring a significant lack of standardization. 66.66% laboratories had not developed specific RIs, relying instead on manufacturer-provided RIs, with infrequent reviews or updates. Challenges were prevalent due to non-harmonized RIs, leading to patient and physician counseling issues. Primary obstacles included funding deficiencies and limited access to healthy samples.

Conclusion: These findings emphasize the critical need for national regulatory guidelines to standardize RIs, thereby enhancing the reliability and accuracy of laboratory diagnostics in Pakistan.

Introduction

Reference intervals (RIs) are integral part of all clinical chemistry laboratory reports. These numerical values are crucial for appropriate interpretation of laboratory results. The International Federation of Clinical Chemistry and Laboratory Medicine (IFCC) has worked relentlessly to provide recommendations for the establishment of RIs helping ensure the quality and accuracy of laboratory testing [1,2]. National Committee for Clinical Laboratory Standards (NCCLS) has published it's guidelines in 2000 [3]. The third edition of C28-A3 guideline (2008) is the latest document for establishment of RI. These guidelines stress on use of a strict evidence based approach by taking samples from local population, with stratifications based on factors such as age and gender, using appropriate statistical method. IFCC Committee on Reference Intervals and Decision Limits (C-RIDL) has proposed new methodologies as a part of global effort to standardize RIs [4]. However, the process of developing RIs is too expensive and labor intensive, a less extensive process that requires only verification of RIs provided by external sources is acceptable. In addition to this the entire process of development or and verification of RIs should be documented and reviewed periodically [5].

Pakistan is a developing country where laboratories have limited resources. Most of Pakistani clinical laboratories opt for RIs mentioned in kit inserts or guidelines that are formulated for Western populations. In addition to this, a wide variation is noted in RIs, reporting units and reporting patterns. These inconsistencies create confusion when comparing results from different laboratories. The regularization of RIs reporting standards is essential to improve reliability, better communication among healthcare providers, and more consistent medical decision-making.

In this nationwide survey, we aim to assess problems faced by laboratory professionals for establishment of RI, find out the extent of the variation in RIs and reporting units used in laboratories across Pakistan for key blood chemistry parameters. By understanding these factors, we can then work towards problem solving and propose recommendations for standardizing reference intervals and reporting practices leading towards better healthcare in Pakistan.

Method

The survey was conducted by the section of Chemical Pathology, Department of Pathology and Laboratory Medicine, the Aga Khan University (AKU), Karachi, Pakistan. We successfully obtained an exemption from the ethical review committee with number 2024-9946-29537. The survey was designed for clinical laboratories performing routine blood chemistry.

A comprehensive e-questionnaire with 30 items was developed using google forms, covering key blood chemistry parameters (Electrolytes, fasting glucose, random glucose, urea, creatinine and lipid profile), reference intervals, reporting units, and laboratory practices. In the first section, four questions were about basic laboratory information. The second section comprised of five questions related to establishment of RIs, three questions were about hurdles and challenges. In the last section, there were 18 questions about units and ranges of key blood chemistry parameters. Within the sections, five questions were multiple choice, allowing the participants to select as many options as they deemed appropriate. Three questions had Yes/No options only. Nine questions were about the units reported while nine were about the specific ranges for each analyte. Importantly, e-mail addresses or internet protocol addresses were not collected.

A list of laboratories performing key blood chemistry parameters (electrolytes, fasting glucose, glucose random urea, creatinine, and lipid profile) across Pakistan was acquired from the marketing department of the clinical laboratory of AKU. Three independent consultant Chemical Pathologists reviewed list, and laboratories were invited by snowball technique, one laboratory invited other laboratory to participate. The inclusion criteria were devised as 1) the laboratory housing a Consultant Pathologist 2) the laboratory is reporting all the parameters being studied in this survey.

The e-questionnaire was administered via email to the participants. Electronic consent for participation was acquired on the initial page of the survey. Participation in the survey was voluntary. The responses were transcribed into Microsoft Excel. Frequency and percentages were calculated for each response and descriptive results (if specified) were evaluated.

Results

A total of 38 responses were received from laboratories across Pakistan. Five responses were excluded due to incomplete forms. Out of the 33 respondents, the participant laboratories were from four provinces and nine cities of Pakistan. The province of Sindh had maximum participation with 17 (51.51%) responses, followed by Punjab 13 (39.39%). All 17 responses from Sindh were from Karachi city only, as presented in Figure 1. As far as lab demographics are concerned 15 (45.45%) were in tertiary care hospitals while only 4 (12.12%) were small community hospital laboratories. Nine (27.27%) laboratories reported an approximate sample workload as more than 1000 samples daily, while another 9 (27.27%) indicated workload between 500-1000, followed by 8 (24.24%) laboratories with 100-250 samples, as shown in Figure 2.

In response to Yes/No questions regarding establishment of RIs, majority of the laboratories 22 (66.66%) had never developed laboratory specific RIs for any of routine blood chemistry parameters. While all the laboratories reported that RIs they used were adjusted for age and gender when necessary. All but one laboratory encountered challenges due to lack of harmonization

of RIs used for routine chemistry analytes. Many laboratories had to individually counsel patients and physicians about the cause of these differences.

In response to multiple-choice questions, it was observed that 5 (15.15%) laboratories never reviewed or updated the RIs, while 24 (72.72%) laboratories claimed to do so when there was a change in analytical method. Manufacturer-provided RIs from assay kits were most commonly used by laboratories across Pakistan. Direct measurement from local samples was rare, and there was no use of Big Data methods. The primary hurdle for establishment of laboratory specific RIs was found to be a lack of funding, followed by limited access to healthy population samples, while lack of time was the least reported issue. The majority of the respondents suggested that national guidelines from regulatory bodies would help in standardizing RIs in Pakistan, as illustrated in Figure 2.

Details of different units and RIs for routine blood chemistry parameters are presented in Table 1, Table 2 and Figure 3.

Figure 1: Map of Pakistan with numbers and locations of laboratory responses.

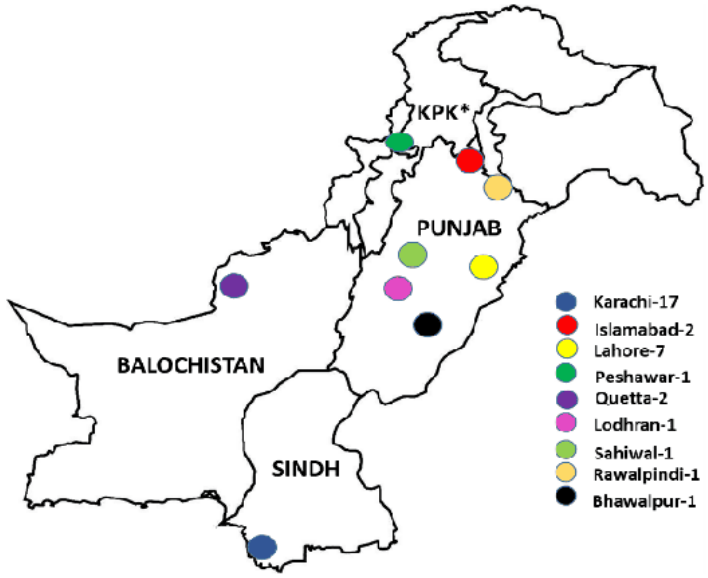

Figure 2: Participant laboratory's demographics and issues faced by laboratories in establishment of reference intervals.

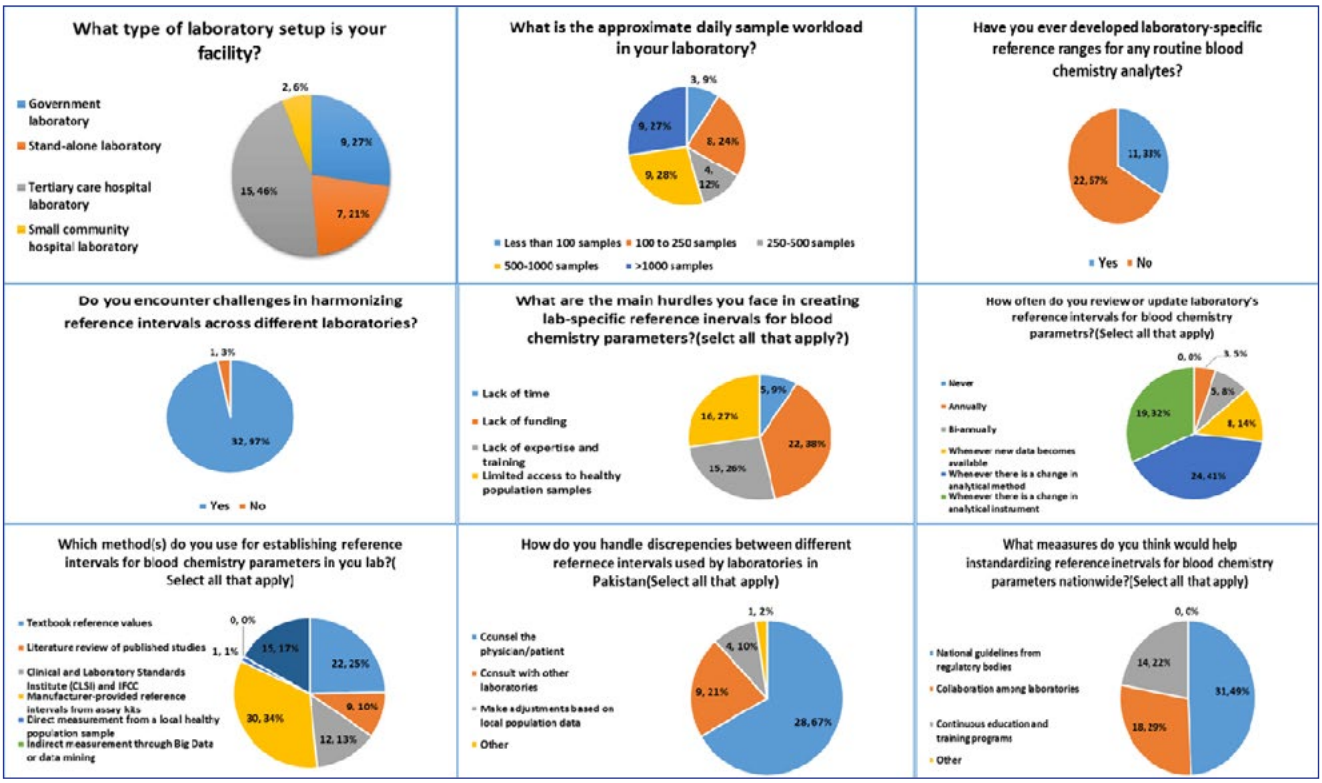

Figure 3: Reference intervals of sodium, potassium and chloride used by different laboratories across Pakistan (concentration unit mEq/L).

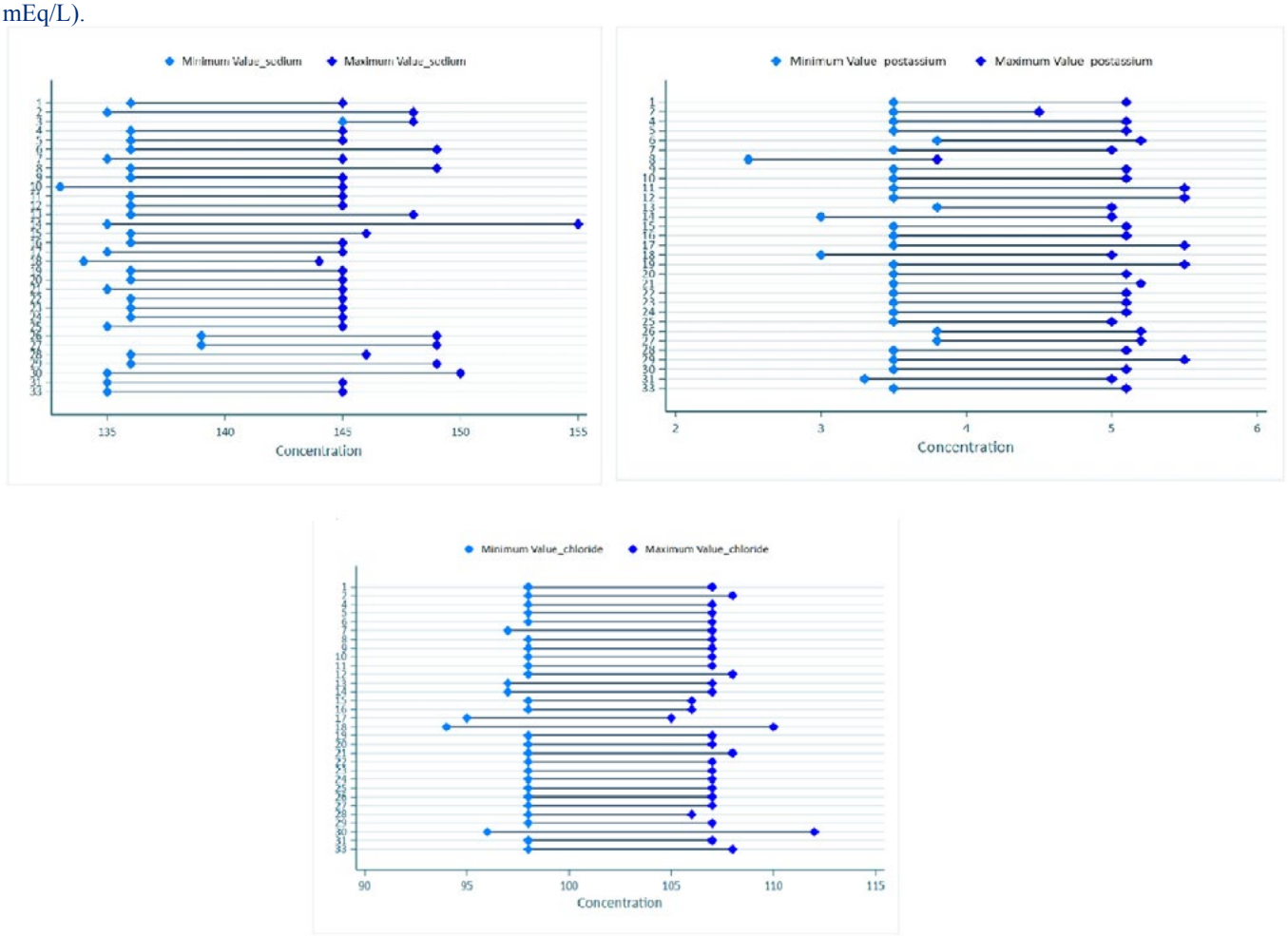

Table 1: Reference ranges and units of glucose, urea and creatinine used by different clinical laboratories across Pakistan.

Respondent lab number	Fasting Glucose, unit	Random Glucose, unit	Serum Urea, unit	Serum Creatinine, unit
Lab no 1	65-100 mg/dl	80-160 mg/dl	6-20 mg/dl	M1.0-1.7 mg/dl F: 0.6-1.3 mg/dl
Lab no 2	70-100 mg/dl	70-140 mg/dl	10-50mg/dl	0.6-1.3 mg/dl
Lab no 3	70 to 99 mg/dl	70-160 mg/dl	10-26mg/dl	0.8- 1.3 mg/dl
Lab no 4	<100 mg/dl	< 140 mg/dl	17-49mg/dl	NB 0.3-1, infant 0.2-0.4, Child 0.3-0.7, Adult M 0.9-1.3, Adult F 0.6-1.1 mg/dl
Lab no 5	Normal <100 Pre diabetes:100 -125 Diabetes:>= 126 mg/dl	<140 mg/dl	6-20mg/dl	Adult M:0.9 - 1.3 mg/dl Adult F :0.6 - 1.1 mg/dl
Lab no 6	Normal FBS 65-100, Impaired FBS >100-<126 Provisional diagnosis of diabetes mellitus >126 mg/dl	<140 mg/dl	10-50mg/dl	0.5-1.5 mg/dl

Respondent lab number	Fasting Glucose, unit	Random Glucose, unit	Serum Urea, unit	Serum Creatinine, unit
Lab no 7	Normal Fasting <100 prediabetes 100-125 Diabetes >126 mg/dl	<140 mg/dl	10-50 mg/dl	0.6-1.5mg/dl
Lab no 8	Normal: 65-100 IFG: 101-125 Provisional diagnosis of diabetes >126 mg/dl	<200 mg/dl	10-50 mg/dl	M 0.6-1.3 F 0.5-1.0 mg/dl
Lab no 10	70-99 mg/dl	<140 mg/dl	15-39 mg/dl	0.5-1.5 mg/dl
Lab no 11	< 100mg/dl	< 200 mg/dl	16.6-48.5 mg/dl	M 0.72-1.25 F 0.57 - 1.11mg/dl
Lab no 12	80 – 110 mg/dl	80 – 180 mg/dl	10-50 mg/dl	0.6-1.3 mg/dl
Lab no 13	70-110 mg/dl	80-200 mg/dl	10-50 mg/dl	M 0.7-1.3 F 0.6-0.9 mg/dl
Lab no 14	70-100mg/dl	<200 mg/dl	10-50mg/dl	M: 0.6 -1.2 F: 0.5-1.1 mg/dl
Lab no15	70-100 mg/dl	70-200mg/dl	6-20mg/dl	M 0.9 1.3 F 0.6-1.1 mg/dl
Lab no16	70-100 mg/dl	70-160 mg/dl	17-43mg/dl	M 0.70 - 1.2 F 0.5 - 0.90 mg/dl
Lab no 17	70-110 mg/dl	140-200 mg/dl	15-45 mg/dl	0.3-1.1 mg/dl
Lab no 18	Normal <100 Impaired 100-125 Diabetes >126 mg/dl	<200 mg/dl	10-50mg/dl	M 0.6-1.2 F 0.5-0.9 mg/dl
Lab no 19	80-110 mg/dl	<140 mg/dl	<40mg/dl	<1.2 mg/dl
Lab no 20	<100 mg/dl	<200mg/dl	12-40 mg/dl	M 0.9-1.3 F 0.6-1.1 mg/dl
Lab no 21	70-110 mg/dl	<140mg/dl	20-45mg/dl	F 0.6-1.1 mg/dl
Lab no 22	70-110 mg/dl	<140mg/dl	10-50mg/dl	M: 0.7-1.2 F: 0.5-1.0 mg/dL
Lab no 23	Normal < 100 IFG 100- 125 DM >126 mg/dl	<200 mg/dl	Adults 13-43 > 60 yrs 17-49 mg/dl	0.5-1.2 mg/dl
Lab no 24	70-99 mg/dl	70-140 mg/dl	9-22mg/dl	M 0.72- 1.25 mg/dl F 0.57- 1.11 mg/dl
Lab no 25	60-100 mg/dl	80-140mg/dl	10-40mg/dl	0.90–1.30mg/dl
Lab no 26	<100mg/dl	70-100mg/dl	10-50mg/dl	0.6-1.1mg/dl M 0.7-1.3 F 0.6-1.1 mg/dl
Lab no 27	Normal <100 IFG 100- 125 DM >126 mg/dl	80- 140mg/dl	17-49mg/dl	M: 0.9-1 mg/dl F: 0.6-1.1mg/dl
Lab no 28	60-100mg/dl	60-200 mg/dl	2.2-7.1 mmol/l	0.5-1.1mg/dl
Lab no 29	Normal <100 Prediabetes 100-125 Diabetes >126mg/dl	DM >200 mg/dl	15-55mg/dl	M 0.75-1.18 mg/dl F 0.55-1.02 mg/dl

Respondent lab number	Fasting Glucose, unit	Random Glucose, unit	Serum Urea, unit	Serum Creatinine, unit
Lab no 30	45 - 99 mg/dl	70 - 140 mg/dl	10-50mg/dl	M: 0.64 - 1.2 F: 0.42 - 1.06 mg/dl
Lab no 31	3.3-5.6mmol/l	<10 mmol/l	Adults: 2.1-7.1 mmol/l	M: 62-120 umol/L F: 60-105 umol/L
Lab no 32	Hypoglycemia <70 Normal 70-99 Pre-Diabetic 100-126 DM >126 mg/dl	Low:< 70 Normal:70-200 High :>200 mg/dl	Low< 10 Normal 10-50 High >50 mg/dl	M:Low <0.73, Normal 0.73-1.18 High >1.18, F: Low< 0.55 Normal 0.55-1.02 High >1.02 mg/dl
Lab no 33	Normal <100 Prediabetes 100-125 Diabetes >126mg/dl	Normal >70 DM >200mg/dl	20-44mg/dl	M:0.9-1.18 F:0.7-0.9 mg/dl

M: male, F: female, DM: diabetes mellitus, IFG: impaired fasting glucose, FBS: fasting blood sugar. NB: newborn

Table 2: Reference ranges and units of lipid profile used by different clinical laboratories across Pakistan.

Respondent lab number	Serum Cholesterol, unit	Serum Triglyceride, unit	Serum HDL cholesterol, unit	Serum LDL cholesterol, unit	Serum VLDL cholesterol, unit
Lab no 1	< 200 without known CAD < 160 with known CAD mg/dl	Normal :<150 Borderline :150-199 High :200-499 Very High: >500 mg/dl	> 40 mg/dl	Optimal: <100 Above Optimal: 100-129 Borderline High:130-159 High: 160-189 Very High: >190 mg/dl	<30 mg/dl
Lab no 2	Desirable: <200 Borderline high: 200-239 High :>240 mg/dl	Normal :<150 Borderline: 150-199 High :200-499 Very high: >500	Low :<40 Desirable: >60 mg/dl	Optimal :<100 Near Optimal: 100-129 Borderline: 130-159 mg/dl	<30 mg/dl
Lab no 3	< 200 mg/dl	< 150 mg/dl	>40 mg/dl	< 130 mg/dl	<30 mg/dl
Lab no 4	Without known CAD< 200 With known CAD< 160 mg/dl	70-150 mg/dl	>35 mg/dl	Without CAD: <150, With CAD: <100 mg/dl	upto 40 mg/dl
Lab no 5	Desirable:<200 Borderline high:200-239 High:>239 mg/dl	Normal:<150 Borderline High:150 - 199 High:200 – 499 Very High:>499 mg/dl	>35 mg/dl	Optimal:<100 Near/above optimal:100 - 129 Borderline High:130 - 159 High:160 – 189 Very High:>189 mg/dl	Not reported
Lab no 6	< 200 without known CAD < 160 with known CAD mg/dl	46-236 mg/dl	Without CAD >40 With known CAD >60 mg/dl	Desirable without CAD <130 Optimal with known CAD <100 mg/dl	Not reported

Respondent lab number	Serum Cholesterol, unit	Serum Triglyceride, unit	Serum HDL cholesterol, unit	Serum LDL cholesterol, unit	Serum VLDL cholesterol, unit
Lab no 7	Normal :<200 Borderline high :200-239 High:>240 mg/dl	Normal: <150 Borderline high: 150-199 High: 200-499 Very high: >500 mg/dl	Optimal: >60 Intermediate :40-60 Low :<40 mg/dl	Optimal: <100 Near Optimal: 100-129 Borderline High :130-159 High :160-189 Very High: 190 mg/dl	Not reported
Lab no 8	Without known CAD < 200 With known CAD < 160 mg/dl	70-150 mg/dl	>35 mg/dl	Without known CAD <150 mg/dl	<30 Calculated mg/dl
Lab no 9	Normal: < 200 Borderline: 201- 239 High :240>mg/dl	Normal :150 Borderline: 151-199 High: 200-499mg/dl	Low risk factor: <40. Desirable >60 mg/dl	Normal: <100 Borderline: 130-159 High: 160-18 Very high: >190mg/dl	<30 normal mg/dl
Lab no 10	<200 mg/dl	Normal:<150 mg/dl	>35 mg/dl	Upto 150 mg/dl	Not reported
Lab no 11	Normal: <200 mg/dl	Normal:<150 mg/dl	< 100 mg/dl	> 60mg/dl	Not reported
Lab no 12	<200 mg/dl	50-150 mg/dl	M:35-55 F:35-65 mg/dl	<100 mg/dl	5.0-30 mg/dl
Lab no 13	140-200 mg/dl	50-200 mg/dl	M:35-55 F:35-65 mg/dl	<150mg/dl	02-30 mg/dl
Lab no 14	Desirable: <200 mg/dl	<150 mg/dl	M: <45 F: <55.0	Desirable: <100 mg/dl	0-25 mg/dl
Lab no15	Desirable:<200 Borderline High: 200-239 High: >239 mg/dl	Normal:<150 Borderline: 150-199 High: 200-499 Very high >500 mg/dl	Low risk factor: <40 Desirable: >60 mg/dl	Desirable: <100 Borderline high: 100-129 High: 130-189 Very high: >189 mg/dl	Not reported
Lab no16	160 - 200 mg/dl	<150 mg/dl	>45 mg/dl	<100 mg/dl	5.0 - 30.0 mg/dl
Lab no 17	<200 mg/dl	<150 mg/dl	M 35-65 F 35-80 mg/dl	100-160 mg/dl	02-30 mg/dl
Lab no 18	<200 mg/dl	50-150 mg/dl	> 40 mg/dl	<100 mg/dl	Not reported
Lab no 19	<200 mg/dl	<150 mg/dl	M>40, F >30 mg/dl	<100 mg/dl	<30 mg/dl
Lab no 20	<200 mg/dl	<150 mg/dl	M > 30 F >34mg/dl	<100 mg/dl	<30 mg/dl
Lab no 21	Desirable: < 200, Moderate: 200-240 High risk :> 240 mg/dl	Desirable: 45- 150 Borderline: 151- 200 High Risk: 201- 500 mg/dl	M desirable: > 60 F desirable 40- 59 Risk, M 50- 59 risk, F: < 40-30 high risk, M< 50 high risk F <30 mg/dl	Desirable: < 100 Above Optimal: 101-130 Borderline High: 131-160 High: 161-200 mg/dl	< 30: Desirable, > 30 mg/dl High

Respondent lab number	Serum Cholesterol, unit	Serum Triglyceride, unit	Serum HDL cholesterol, unit	Serum LDL cholesterol, unit	Serum VLDL cholesterol, unit
Lab no 22	Normal: <200 Borderline high: 200-239 High: >240 mg/dl	Normal: 100-130, Borderline: 130-160 High> 160mg/dl	35-50mg/dl	50-150 mg/dl	Not reported
Lab no 23	Desirable :> 200 Borderline :200- 239 High :> or equal to 240 mg/dl	<150 mg/dl	Less than 40 (low)mg/dl	<100 mg/dl	Not reported
Lab no 24	Less than 200 mg/dl	Less than 150 mg/dl	Greater than 40	Less than 130 mg/dl	Less than 30 mg/dl
Lab no 25	<200 mg/dl	<150 mg/dl	>45 mg/dl	<130 mg/dl	Not reported
Lab no 26	<200 mg/dl	<200 mg/dl	>40 mg/dl	100-129 mg/dl	<40 mg/dl
Lab no 27	Desirable: <200 Borderline: 200-239 High:>239 mg/dl	<150 normal mg/dl	M> 40. F> 50 mg/dl	Optimal: <100 Above Optimal :100-129 Borderline High: 130-159 High: 160 -189 Very High: >190 mg/dl	Calculated
Lab no 28	140-200 mg/dl	50-150 mg/dl	40-70 mg/dl	70-100 mg/dl	Not reported
Lab no 29	Desirable without CAD <200 Optimal with CAD < 160 mg/dl	<150 mg/dl	without CAD: >40 with CAD: >=60 mg/dl	Desirable without CAD: <130 Optimal with CAD <100 mg/dl	Not reported
Lab no 30	< 200 mg/dl	< 200 mg/dl	35 - 65 mg/dl	< 150 mg/dl	Not reported
Lab no 31	Desirable <5.2 mmol/L	0.4 to 1.6 mmol/L	>1.3 mmol/L	<2.59 mmol/L	0 to 0.78 mmol/L
Lab no 32	Desirable: <200 Borderline high: 200-240 High: >240 mg/dl	Normal :<150, Borderline high: 150-199 High: >200-499 Very High >500 mg/dl	Low <39, Normal > 40 mg/dl	Desirable :<100 Above Desirable:100-129 Borderline high:130-159 High:160-189 Very High: >190 mg/dl	Desirable: <129, Above Desirable: 130-159, Borderline high: 160-189, High: 190-219 Very High: >220 mg/dl
Lab no 33	Desirable :<200 Borderline high: 200-240 High: >240 mg/dl	Normal:<150 Borderline : 150199 High: 200 -499 Very high: >500 mg/dL	Low < 40 Normal >50	Near optimal: 100 - 129 Borderline high: 130 -159 High: 160 -189 Very high: >190 mg/dl	<40 mg/dl

M: male, F: female, HDL:high density lipoprotein, LDL: low density lipoprotein, VLDL: very low density lipoprotein, CAD: coronary artery disease

Discussion

Reference intervals reported along with each analyte are considered as important as the actual observed value [6]. Due to differences in lifestyle components, dietary habits and genetic makeup it is recommended to use region specific, or laboratory validated RIs in clinical laboratory reports [7]. However, RIs among Pakistani population are not clearly defined and most laboratories rely heavily on RIs established for Caucasian population. Harmonization of RIs is essential to ensure standardized health care.

In our survey, we found that most of the laboratories were affiliated with tertiary care hospitals with a large workload of more than 500 samples daily. Despite this high volume, it was alarming to note that two thirds of the laboratories had never established their own RIs for any routine blood chemistry parameters. The standard recommendation is to select a minimum of 120 healthy reference subject for establishment of RIs. This process is very tedious, so a simpler method of RIs verification can be done with only 20 healthy subjects [5]. While all of the respondents were using age and gender adjusted RIs, many faced difficulties due to variabilities in RIs used by different laboratories. These inconsistencies can potentially lead to confusion and errors in diagnosis and treatment. There is an urgent need for consolidated efforts for establishment/verification of population specific RIs.

Establishment of RIs is a difficult, expensive and time intensive project and laboratories in lower-middle income countries like Pakistan face several difficulties in the process [8]. Financial constraints was reported as the primary barrier, cited by 22 respondents. Funds are required for reference population selection, kits, and staff training. The second biggest problem was found to be a lack of expertise and training. Training in data interpretation and data analysis is critical for reliable RIs. The respondents also found it difficult to get samples from healthy population as they mostly dealt with patients suffering from one disease or another. Time constraints were the least cited but still relevant issue. All this highlights the urgent need for national level consolidated efforts for monetary support, training programs and better sample collection strategies.

It was interesting to note that none of the laboratories reported that they never reviewed or updated their RIs. This indicates that all laboratories have a recognition for updated RIs. However, most of the laboratories only updated RIs whenever a new analytical method was introduced, followed by any change in analytical instrument. Very few laboratories had a routine of annual RIs review. This lack of periodic review may be insufficient for accurate reporting.

The laboratories used RIs from various sources. Manufacturer-provided RIs from assay kits were most widely used. These values are specific to instrument and reagent used, and not formulated to population specific needs. Textbook RIs are readily available and were found to be next most popular option. Less than half laboratories reported using (CLSI), IFCC national or international guidelines, this may be due to a general lack of awareness about their availability. Only one laboratory employed the direct method for establishment of RIs using local healthy population. This method is least used as it needs a significant time and effort. Although many laboratories had very large sample volume, none of the laboratories opted to big data or indirect data mining. Big data employs multiple statistical tools for calculation of RIs [9]. The absence of its use may reflect a lack of infrastructure, expertise, or access to large datasets required for effective implementation. These limitations must be addressed for enhancing clinical laboratory reporting.

Many patients need serial monitoring of blood chemistry parameters for disease and treatment monitoring [10,11]. Patients may get the same tests from different laboratories over the years. 32 (96.70%) laboratories faced challenges due to variations in RIs of same analyte. Managing such discrepancies required multifaceted approach. The most common approach, used by laboratories was to counsel the physician or patient about the causes of such variations. Only a small portion of laboratories consulted with other laboratories or made adjustments based on local population data. Such discrepancies in unnecessary confusion for patient and extra work for laboratory professionals.

When asked about their opinion for various measures to standardize RIs across Pakistan, an overwhelming majority believed that national guidelines from regulatory bodies would be instrumental in standardizing RIs nationwide. A significant portion recognized that collaboration among laboratories and continuous training programs for better standardization of RIs. This points towards urgent need for consolidated nationwide efforts across government and public sectors to establish guidelines RIs for Pakistani population. These guidelines will provide a benchmark for laboratories to follow, promoting consistency and quality assurance in diagnostic practices.

When we analyzed our responses for RIs of serum sodium we found that majority of the laboratories [12 (54.50%)] use the range 136-145. This indicates a strong preference for this reference interval. Other laboratories also reported roughly similar RI for serum sodium. The most frequently reported range of potassium is 3.5-5.1, with 11 (33.33%) adhering to this range. Other ranges include 3.5-5.5 mEq/L [5 (15.15%) laboratories], 3.0-5.0 mEq/L [4 [12.12%] laboratories), 3.8-5.2 mEq/L [4 [12.12%] laboratories), and 3.5-4.5 mEq/L [1 [3.03%] lab)]. The most frequently reported range for serum chloride is 98-107 mEq/L or mmol/L [21 (63.63%) laboratories]. Other ranges were roughly similar with two outliers, which were 95-105 mmol/L and 96-112 mmol/L. There is a notable split between mEq/L and mmol/L, with both being used almost equally across the board. Electrolytes play a vital role in controlling the acid base balance, nerve conduction, muscle contraction and enzyme

activity within the body. Electrolyte disorders are commonly encountered in clinical practice [12, 13]. Different RIs and units used by various laboratories can lead to confusion and potential diagnostic errors.

The most frequently reported range for fasting glucose was 70-100 [8 (24.24%) laboratories]. Other reported ranges include 65-100 [2 (6.06%) laboratories], 70-99 [2 (6.06%) laboratories], and 70-110 [2 (6.06%) laboratories]. Only a few laboratories adopted a more detailed reporting approach with specific classification like Normal [10 (30.30%) laboratories)], Pre-diabetes [5 (15.15%) laboratories], impaired fasting glucose [4 (12.12%)], provisional diagnosis of diabetes [3 (9.09%)] and Diabetes [7 (21.21%) laboratories]. There was variation among RI for normal and pre-diabetic/impaired fasting glucose; however, diabetes was labelled at > 126 mg/dl by all laboratories. For random glucose the most frequently reported range was <140 mg/dL, reported by [8 (24.24%) laboratories] followed by <200 mg/dL [5 (15.63%) laboratories]. There was variability in the upper and lower limit of random glucose reporting, with some laboratories providing upper limits as high as 200 mg/dL and lower limit as 60mg/dl. One laboratory gave detailed RIs as Low< 70, Normal 70-200 High >200 mg/dl and one lab reported Normal >70 diabetes >200 mg/dl. Only one lab used the unit as mmol/l while all the rest used mg/dl as the reporting unit. Several guidelines are available for diagnosis and monitoring of diabetes mellitus that depend upon levels of fasting and random glucose [14, 15]. Variations in RIs for fasting and random glucose levels across different laboratories can have significant implications for the diagnosis, management and monitoring of diabetes and potentially cause patient safety issues.

The most frequently reported RI for serum urea was 10-50 mg/dL, reported by 14 (42.42%) laboratories. There was a variation in the upper limit ranging from 22-50 mg/dl. Two laboratories reported in mmol/l rest used mg/dl as the unit. Only one laboratory reported as low, normal, High, while the rest used only a single RI with no further specifications. For serum creatinine 20 (60.60%) stratified RI for gender, 1 (3.03%) stratified according to age and 1 (3.03%) stratified as low, normal and high. Considerable variation was noted in lower limit (0.3-1.0mg/dl) and upper limit (1.0-1.7 mg/dl). The commonly used reporting unit was mg/dl. Serum urea levels are used to assess the state of hydration and kidney function in body in the body. Differences in RIs for urea and creatinine can lead to variability in diagnosing renal dysfunction or dehydration. In addition to assessment of renal functions, creatinine levels are crucial for dosing medications that are renal excreted. Variations in RIs can result in either underdosing or overdosing medications, particularly in drugs with narrow therapeutic indices [16, 17].

While analyzing lipid profile, a wide variation in RI was noted. In addition to this, only 5 (15.15%) laboratories mentioned RI stratified according to coronary artery disease (CAD), 10(30.30%) laboratories stratified serum cholesterol results as desirable, borderline high and high. Serum triglyceride (TG) was reported as normal/desirable, borderline, high /very high by 10 laboratories. Most commonly reported RI for normal was 150 mg/dl. For serum High-density lipoprotein (HDL) various terms like optimal/ desirable, intermediate, low, low risk factor, risk, high risk. 8 (24.24%) laboratories had gender stratification. A wide variation was noted in the reported optimal RI (>35->60mg/dl). For serum low density lipoprotein cholesterol (LDL) 4(12.12%) laboratories mentioned RI stratified according to CAD, various terms like optimal/near optimal/above optimal/ desirable, borderline/ borderline high, high, very high, low, low risk factor, risk, high risk were used. Wide variation was noted in desirable /optimal RI (>60- <150 mg/dl). 13 (39.39%) laboratories did not report VLDL.

Conclusion

The survey highlights significant challenges faced by clinical laboratories in Pakistan regarding the establishment of RIs. There is wide variation in RIs across different laboratories, which may lead to inconsistencies in diagnostic practices and cause patient safety issues. There is urgent need for national guidelines and collaborative efforts to standardize RIs, ensuring accurate and consistent diagnostic outcomes across all laboratories in Pakistan.

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