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LIMITATIONS OF SELECTED LABORATORY PARAMETERS AND ITS INTERPRETATION ON PATIENT DIAGNOSIS

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ABSTRACT

Laboratory tests are procedures, usually conducted in a laboratory, that is intended to detect, identify or quantify one or more significant substances, evaluate organ functions, or establish the nature of a condition or disease. Laboratory testing is a highly intricate process and is comparatively safe. Indeed their occurs some laboratory errors due to poor conveying. The most recent investigation on errors in laboratory testing terminate that in the consignment of laboratory examination, mistakes occur more often before (pre-analytical) and after (post-analytical) the test has been performed. Majority errors are due to pre-analytical factors (46-68.2% of total errors), while an inflated error rate (18.5-47% of total errors) has also been found in the post-analytical errors. Errors due to analytical complications may have a significant effect on patient diagnosis. In present-day approach to total quality, entered on patient's necessity and contentment, the possibility of errors must be diminished to assure the total quality of laboratory services. An estimated 60% to 70% of all decisions concerning a patient's diagnosis and therapy are based on laboratory test outcomes. All the commonly used laboratory parameters like liver function tests, renal function tests, haematological tests, thyroid function tests, lipid profile tests, cardiac biomarker, and electrolytes are taken for the following study.

Key words: Laboratory tests, Pre-analytical errors, Post-analytical errors, Laboratory parameters.

INTRODUCTION

Clinical laboratory examination plays a crucial role in the delivery of quality health care through right diagnosis and promoting Rational prescriptions. A physician or other clinician instructs the laboratory examination to diagnose, treat, control or observe the patients' health status [1]. Few tests are manually assessed, while majority of the tests are conducted using technically advanced equipments. They recruit groups of authorized, immensely skilled and experienced medical professionals particularly trained to conduct the laboratory tests. Missed diagnosis or incorrect diagnoses had a central role in medical education, research and quality assurance in the form of autopsies and also include malpractice litigation, morbidity and mortality. The important aspects that affect test results are correlated with ageing along with increasing co morbidities and poly pharmacy [2-6]. The outcome of age, gender and other factors on interpretation of laboratory results is Serum alkaline phosphatise as it significantly increase during puberty as this is the period of bone remodelling[7]. A patients calorie intake, food banning, lack of proper nutrition's, lack of body fluids can all effect laboratory outcomes like fasting 12 hours prior to laboratory testing may be useful or even essential while testing the Serum creatinine levels as a high meal content can have a remarkable impact on the serum creatinine levels as well as fasting may not be necessary for certain laboratory tests like HbA1c, triglyceride levels, uric acid levels. Malnutrition like under nutrition, over nutrition or deficiency can be considered as a cause in varying laboratory results like ferritin, folate and vitamin B12 deficiency. Dehydration can be considered as a cause of sodium and potassium imbalances and can also affect

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Creatinine, urea, albumin, lipids and haematology results. The effect of alcohol consumption on laboratory investigations depends on the duration and extent of use. Acute alcohol consumption includes decreased serum glucose. Chronic effects of alcohol consumption on laboratory result include elevated levels of GGT, MCV, AST, ALT, triglyceride levels, anaemia, and fatty liver, alcoholic hepatitis. Tobacco smoking have an acute and chronic effects on laboratory results like leukocyte counts, PCV levels can be decreased in the activity of some enzymes. Medicines like Proton pump inhibitors, Antibiotics, NSAIDs can significantly affect the laboratory results. Creating and maintain a patient problem list can help prevent diagnostic errors [8].

LIVER FUNCTION TESTS

Serum Albumin:

Serum Albumin is useful in assessing the nutritional status, chronic illness, liver disease. Serum Albumin increases in dehydration and high-protein diet as well as decreases in acute and chronic liver disease, Amyloidosis, diabetes mellitus, Hypothyroidism, Peptic ulcer, Kidney disease, Haemorrhage, insulin, anabolic steroids and growth hormone can affect the results of the test. Large amounts of intravenous administration leads to the inaccurate test results. This can be prevented by regulating the synthesis of albumin with a variety of influences including nutritional status, serum oncotic pressure, cytokines and hormones [9].

Alkaline Phosphatase:

Alkaline phosphatase is effective in identifying and preventing the liver, bone, intestinal and parathyroid diseases. Alkaline phosphatase increases in bone diseases, renal diseases, ulcerative colitis, penicillin derivatives, anti-epileptic drugs, antihistamines, cardiovascular drugs and decreases in hypophosphatemia, pernicious anaemia, vitamin B12 deficiency, corticosteroids, trifluoperazine. A rise in ALP levels inclined to be clearer in extra hepatic biliary obstruction than in intra hepatic obstruction.25% higher with increased body mass index, 10% higher with smoking, 20% lower with the use of oral contraceptives. This can be prevented by fasting 10 hours before the test. Because eating can interfere the ALP levels [10].

Aminotransferases (AST and ALT):

AST is primarily found in heart, liver, skeletal muscle and kidney whereas ALT is primarily found in liver and kidney. Majority of the sensitive tests for acute hepatocellular injury precedes rise in serum bilirubin by approximately 1week. Aminotransferases increases in hepatocellular damage, alcoholic hepatitis, acute heart failure, burns, stroke and decreases in azotemia, chronic renal dialysis, malnutrition. It is rarely asymptomatic with ALT and AST levels >1000U/L. AST >10 times usually signifies acute hepatocellular injury, but minor rise in the level of AST are nonspecific and may occur with almost any type of liver injury. A rise in (<8 times) upper limit of normal are nonspecific; may be found in any liver disorder. Rarely increased >500 U/L in post hepatic jaundice, AIDS, cirrhosis and viral hepatitis. Chronic and acute alcohol use also can commonly cause abnormal liver blood tests. NSAIDs, anti-seizure drugs, antibiotics, statins and cardiovascular drugs can be responsible for mild to moderate increase in liver enzyme tests. These medications should be avoided. Liver biopsy is useful in confirming a diagnosis of a potentially treatable condition [11].

Serum Bilirubin (Total, Direct and Indirect):

Serum Bilirubin is useful in assessing the liver function, range of diseases affecting the production, uptake, storage, metabolism or excretion of bilirubin, the efficacy of neonatal phototherapy. Serum Bilirubin increases in hepatocellular damage, biliary obstruction, haemolytic disease, hereditary disorders and decreases in barbiturates. Specimens should be protected from light and analyzed as soon as possible. Light exposure can decrease total bilirubin up to 50% per hour. Total serum bilirubin not a sensitive indicator of hepatic dysfunction; it may not reflect degree of liver damage. Medications that affect bilirubin levels include antibiotics, sedatives, diuretics and Anti-asthmatic medications. These drugs should be avoided. Before the test is performed should not eat or drink anything other than water for four hours. Day to day variations is 15-30% and increases an average of 1-2 folds with fasting up to 48 hours [12].

Total Serum Protein

Serum protein is effective in identifying and preventing the diseases involving liver, kidney, bone marrow, screening for nutritional deficiencies. Serum protein increases in hypovolemic states and decreases in nutritional deficiency, decreased protein synthesis, GI disease, and skin disease. Falsely elevated proteins can be caused by hemoconcentration due to dehydration or sample desiccations. A person sitting in upright posture for several hours after rising from bed helps to increase total proteins and several other analysts [12].

LIPID PROFILE TESTS

Lipid profile tests are useful in assessing the risk of heart disease and atherosclerosis. HDL level increases in hyperalphalipoproteinemia, regular physical activity, weight loss, chronic liver disease and it occur due to moderate ethanol consumption, estrogens and insulin. HDL level decreases in uncontrolled diabetes, cholestasis, deficiency of Apo A-1 and Apo C-III and it occurs due to starvation, stress, recent illness, smoking, and obesity, lack of physical activity, drugs such as steroids, thiazide diuretics, beta blockers and elevated serum immune globulin levels [13]. LDL levels are Increased in familial hyper cholesterolemia, nephritic syndrome, hepatic disease,

chronic renal failure because of a diet high in saturated fats, cholesterol, pregnancy or use of steroids [13]. LDL levels decreases in hyperthyroidism, chronic anaemia, Apo C II deficiency. Total cholesterol levels increases in obesity, smoking, alcohol, beta blockers, vitamin D, oral contraceptives, and hepato cellular disease. Total cholesterol levels decreases in malnutrition, liver disease, chronic anaemia, infection, stress. Intraindividual variation up to 10%. Seasonal variation up to 8% higher in winter than summer. Triglyceride levels increases in hypolipoproteinemia, diabetes, nephritis, pancreatitis, liver disease, corticosteroids, and beta blockers. Triglyceride levels decreases in malnutrition, malabsorption, and hyperthyroidism. This can be prevented by taking only the fasting samples and patient should avoid consumption of alcohol, smoking and take proper nutritious food [14].

CARDIAC BIOMARKERS

CK-MB:

CK-MB plays an important role as an early marker for myocardial injury. CK-MB increases in AMI, myocarditis, cardiomyopathies, coronary angiography, skeletal muscle diseases, bacterial, viral infections, aspirin, tranquilizers, muscular dystrophies, polymyositis, hypothermia, renal failure, tissue damage, cardiac contusion and decreases in angina pectoris, IM injections, and seizures. Cardiac troponin is the most favoured marker for the identification of MI. CK-MB by mass assay is an acceptable substitute when cardiac troponin is not accessible [15].

Cardiac Troponins (T and I):

Cardiac troponin is the preferred test for the diagnosis of acute coronary syndrome, myocardial infarction and other heart diseases. Cardiac troponin increases in hypotension, myocarditis, renal failure, doxorubicin, and 5-flurouracil. Troponin is able to detect very early stages of disease and confer a worse prognosis if elevated, if confounding factors for laboratory analysis of troponin are suspected, the use of other cardiac biomarkers in addition to direct cardiac imaging is strongly recommended [16].

Serum C - reactive protein (CRP):

CRP is used for evaluating infection, tissue injury and inflammatory disorders. Independent risk factor for atherosclerosis, cardiac vascular events, hypertension and MI. CRP level increases in rheumatoid arthritis, cardiovascular disease, oral contraceptives, osteomylitis and decreases in patients treated with carboxypenicillins, liver failure. Elevated CRP values are nonspecific and should not be interpreted without a complete clinical history. Heterophile antibodies may falsely increase levels. This can be prevented by following a sedentary life style, and avoid stress, exposure to environmental toxins and diet that specifically contains refined, processed and manufactured foods [17].

BLOOD GLUCOSE TESTS:

OGTT: (Oral glucose tolerance test)

OGTT is useful in the diagnosis of gestational diabetes mellitus. In the absence of unequivocal hyperglycaemia with acute metabolic decomposition, these criteria should be confirmed by repeat testing on a separate day.OGTT is not used for a routine clinical use. Prior diet of >150g of carbohydrate daily, no alcohol and unrestricted activity for 3 days before the test. Oral diuretics, oral contraceptives, and phenytoin should be avoided.OGTT is not recommended in children, persistent fasting hyperglycaemia and persistent fasting normal glycaemia [18].

Blood Glucose:

Blood glucose is used in the diagnosis of DM, hypoglycaemia, gestational DM. Blood glucose levels increases in hemochromatosis, acromegaly, stress, acute pancreatitis, corticosteroids, estrogens, phenytoin, thiazide, propranolol, strenuous exercise, strong emotions, shocks, burns, infections and decreases in glucagon deficiency, hepatitis, endocrine disorders, and oral hypoglycaemic medications. Blood samples in which serum is not separated from blood cells show decreased glucose levels. This can be prevented by fasting before the test is being performed because they provide more accurate results and are easy to interpret [19].

Haemoglobin A1C: (Hematocrit)

Hematocrit is useful in monitoring compliance and long term blood glucose level control in patients with diabetes, index of diabetic control, predicting development and progression of diabetic microvasculature complications. Hematocrit levels increases in chronic renal failure, iron deficiency anaemia, splenectomy, and salicylate treatment and decreases in shortened RBC life span, hemoglobinopathies, and ingestion of large amounts of vitamin C or E [20].

Electrolytes

Sodium is used in the diagnosis and treatment of dehydration and over hydration, acid-base balance, water balance, water intoxication. Sodium increases in conditions associated with water loss, GI loss of fluid, diabetes insipidus, burns or excessive sweating, loop diuretics, osmotic diuretics and decreases in hyponatremia, renal loss of sodium and water. Serum sodium decreases 1.7 mEq/L for every increase of serum glucose of 100mg/dl.[21] Potassium is used in the evaluation of electrolyte balance, cardiac arrhythmia, muscle weakness, hepatic encephalopathy, renal disease, hyperkalemia and hypokalemia. Potassium level increases in potassium

retension, primary tubular disorder, decreased insulin, beta adrenergic blockade,digitalis,mannitol and decreases in excess renal excretion, renal tubular acidosis, endocrine disorders, diuretics, flurocortisone, penicillin, amino glycosides[21]. Calcium is used in the diagnosis and monitoring of a wide range of disorders, including disorders of protein and vitamin D, and diseases of the bone, kidney, parathyroid gland or GI tract. Calcium level increases in acute and chronic renal failure, osteomalacia, malabsorption, estrogens, androgens, progestin, lithium and decreases in hyperparathyroidism, hereditary, respiratory alkalosis, cancer drugs, anticonvulsants, antibiotics, loop diuretics [21]. Total serum protein albumin should be measured simultaneously for proper interpretation of serum calcium levels. Chloride is used with sodium, potassium and carbondioxide to assess electrolyte, acid-base and water balance [21]. Chloride levels increases in renal tubular diseases, dehydration, and respiratory alkalosis, salicylate, acetazolamide, and diabetes insipidus and decreases in prolonged vomiting, adrenocortical insufficiency, furosemide, thiazide, ethacrynic acid. This slightly decreases after meals; fasting specimen collection is recommended [21]. BICARBONATES are significant indicator of electrolyte dispersion and anion deficit. Together with pH determination, bicarbonate measurements are used in the diagnosis and treatment of numerous potentially serious disorders associated with acid-base imbalance in the respiratory and metabolic systems [21]. Some of these conditions are diarrhoea, renal tubular acidosis, carbonic anhydrase inhibitors, hyperaemic acidosis, renal failure and ketoacidosis. Bicarbonate level increases in severe vomiting, COPD, diuretics, respiratory acidosis, barbiturates, hydrocortisone, loop diuretics, steroids and decreases in salicylate overdose, chronic diarrhoea, metabolic acidosis, methicillin, tetracycline, nitrofurantoin and thiazide diuretics [21]. Bicarbonate can be determined by titration, but this is rarely done. Serum magnesium is used in diagnosis and monitoring of hypomagnesaemia and hypomagnesaemia especially in renal failure or GI disorders, to monitor preeclampsia patients, being treated with magnesium sulphate. Magnesium level increases in laxative and cathartic abuse, parenteral nutrition, diuretics, antacids and decreases in malabsorption, phosphate depletion, antineoplastics, cyclosporine, and extracellular fluid volume expansion. Serum magnesium remains normal even when total body stores of magnesium are depleted up to 20%.Phylate, fatty acids and an excess of phosphate impair magnesium absorption [21].

RENAL FUNCTION TESTS

Blood Urea Nitrogen (BUN):

BUN plays an important role in diagnosing the kidney function along with serum creatinine. BUN levels helps in the diagnosis of prerenal, renal, post renal hyperaemia, renal insufficiency, and glomerular function. Provides evidence of haemorrhage into the upper GI tract. BUN levels increases in impaired kidney function, CHF, shock, stress, Corticosteroids, tetracycline and decreases in diuresis (over hydration), severe liver damage, diet (low protein and high carbohydrate). The presence of ammonium ions in anticoagulants may produce falsely elevated results [22].

2. eGFR

eGFR is useful for altering the doses of renally impaired patients. It increases in diet, muscle disease, pre and post renal azotemia, aminoglycosides and penicillin and decreases in pregnancy, reduced skeletal muscle mass, cimetidine, trimethoprim, enzymatic reaction, ketoacidosis, cephalosporin's, ascorbic acids. A laboratory specialist should take into account all the factors like age, gender, height to calculate the most accurate results [22].

3. Uric Acid:

Uric acid plays an important role in identifying and treating gout, observes the chemotherapeutic treatment of neoplasm to evade renal urate deposition with feasible renal failure. Uric acid level increases in polycythemia, asymptomatic hyperuricemia, multiple myeloma, nitrogen mustards, vincristine, prednisone and decreases in Wilson's disease, acromegaly, salicylate, probenicid, allopurinol, and indomethacin. Rapid degradation of uric acid occurs at room temperature. Blood should be collected in prechilled tubes and centrifuged and it should be analyzed within 4 hours of collection [23].

Haematology Tests:

RBC is used in the diagnosis of anemia.RBC level increases in myeloproliferative neoplasms, severe dehydration and decreases in various types of anaemia. WBC is the important part of the immune system. These cells help fight infections by attacking bacteria, viruses, germs. WBC level increases in infection, anemia, leukaemia, stress, exercise, tissue damage, allergy and decreases in HIV, autoimmune disorders, liver and spleen diseases. With the recent introduction of automated equipment for reporting of differential counts this bias has been minimized. Platelet count is used in the diagnosis of thrombocytopenia. Platelet levels increases in clonal bone marrow disorders, acute haemorrhage, and chronic inflammatory disorders and decreases in aplastic anaemia, thrombocytopenia, and leukaemia. Interference and limitations are more numerous with platelets than with RBC and WBC. Platelets cannot be accurately counted after being stored at 4 degree centigrade for more than 24 hours, so temperature should be maintained appropriately. ESR is used to monitor the course or response to therapy of diseases ESR level increases in infection, renal disease, anaemia, inflammatory arthritis, aging and decreases in sickle cell anaemia, polycythemia Vera, CHF, typhoid, peptic ulcer [24].

OTHER TESTS

Serum Iron:

Iron is used in the diagnosis of blood loss, anaemia, and acute iron toxicity. Increases in idiopathic hemochromatosis, repeated transfusions, lead poisoning, and acute hepatitis and decreases in acute and chronic infection, carcinoma, nephritis and hypothyroidism. Not recommended for patients undergoing treatment with deferoxamine or other iron chelating compounds. Ingestion of irons may cause transient elevated iron levels [25].

Total Iron Binding Capacity:

TIBC is used in the diagnosis of anaemia, screening for overload, acute hepatitis and late pregnancy. TIBC levels increases in iron deficiency anaemia, progesterone birth control pills, acute liver damage, oestrogens, oral contraceptives and decreases in hemochromatosis, cirrhosis of liver, asparaginase, chloramphenicol, corticotrophin, cortisone and testosterone decrease the TIBC levels. Fasting of eight hours is required for a TIBC test to ensure the most accurate results [25].

Thyroid Function Tests:

Triiodothyronine (T3) is used to diagnose the hypothyroidism patients. Increases in severe non thyroidal illness except in some liver disorders, HIV, renal Failure and decreases often in hypothyroidism but overlaps with normal range. TOTAL THYROXINE is used in the diagnosis of hyper and hypo thyroidism due to pituitary and hypothalamic diseases. Increases in pregnancy, estrogens, birth control pills, amiodarone, amphetamines and decreases in nephrosis, cirrhosis, phenytoin, triiodothyronine, and corticosteroids [26].

CONCLUSION

Diagnosis errors are challenging to detect and dissect. The main factors that affect the laboratory parameters are age, gender, physiological conditions, sampling methods, storage conditions, method of analysis. To avoid laboratory errors or to obtain error free diagnostic results, effective and efficient follow up of abnormal test results, standardising protocols for reading lab tests particularly in training programs. The clinicians and physicians of laboratory can expand their mission from a factory model focused almost exclusively on providing accurate, timely test results at the lowest possible cost that enables the accurate diagnosis of conditions, selection of appropriate treatment, effective monitoring of health status. These ideas need to be tested and implemented for more timely and error free diagnosis.

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