INTERNATIONAL JOURNAL OF CURRENT MEDICAL AND PHARMACEUTICAL RESEARCH

IJCMPR

ISSN: 2395-6429

Available Online at http://www.journalcmpr.com

DOI: http://dx.doi.org/10.24327/23956429.ijcmpr20170001

RESEARCH ARTICLE

INDUCED PLASMA ELECTROLYTES IMBALANCE IN OMEPRAZOLE AND ANTACIDS TREATED GASTRIC ULCER

Jimmy E. O[1] and Bassey A. I[2]

Department of Physiology, Faculty of Basic Medical Sciences, University of Uyo, Akwa Ibom State, Nigeria

ARTICLE INFO

Article History:

Received 12th December, 2016
Received in revised form 7th January, 2017
Accepted 26th February, 2017
Published online 28th March, 2017

Key words:

Electrolyte levels, Omeprazole, Antacids, Gastric Ulcer.

ABSTRACT

The effects of Omeprazole and antacids on electrolytes level were investigated in twenty-four (24) male and female matured rats induced with gastric ulcer for 30 days. The study was divided into 6 groups. Group 1 – control, Group 2 – Ulcer without treatment while 2 – 5 groups were given combined treatments (Omeprazole and Antacids) group 6 had only omeprazole treatment. Sodium, Potassium, calcium chloride and bicarbonate were the electrolytes assayed.

Plasma sodium was higher in group 6 ($p<0.05$) than other groups while sodium in group 5 was insignificantly different from groups 1,2,3,4 and 6 ($p<0.05$). The mean potassium was different between the groups, ($p<0.05$) and potassium in group 2 was significantly higher than the entire group ($p<0.05$). Magnesium in group 3 was significantly higher than groups 1 and 2, ($p<0.05$) while in groups 4, 5 and 6 magnesium were significantly less than that of group 2 and 3 ($p<0.05$). There was a significant increase in calcium in groups 5 than those of groups 1, 2, 4 and 6 ($p<0.05$). There was also a significant decrease in bicarbonate level in group 3 than group 1, ($p<0.05$), but the value in group 5 was significantly less than in group 1 and 4 ($p<0.05$). Chloride in group 2 was higher than group 3 ($p<0.05$) while those of group 4, 5, and 6 were less ($p<0.05$). It is shown in the study that therapy of omeprazole and antacids in ulcer treatment vary the electrolytes concentration which may affect body function.

INTRODUCTION

Gastric ulcer is a gastrointestinal tract disease characterized by ulceration or perforation or sore on the mucosal lining of the tract. Guyton, 2006; Oyebola, 2002.

There is alarming rate of incidence of the peptic ulcer globally (WHO, 1999) but a greater proportion of this is not documented. In Nigeria, it is 10 – 15% (Olubuyide,(1989)) but the global incidence is higher.

Gastric ulcer is caused by; helicobacter pylori, drugs, alchoholism, HCL production, smoking, (tripathi, (2008)); (Maiden, (2002)); (Maa, (2000)); Boekema, (1999). It is also caused by food eg. Tea and coffee and raised gastrin and HCL (Jimmy, (2013)), Guyton, 2006. However, the HCL related gastric ulcer is a function of gastric vulnerability, integrity, resistance, autonomic impulses, local vascularity and gastro-duodenal barrier since not all cases of high Hcl induces gastric ulcer. Gastric may be caused by stress as stress lowers the mucosal blood flow and thus suppressing the mucus protecting synthesis. Adrenocortical response to stress lead to reduced resistance to infection e.g. Gastritis often results in gastric ulcer, (Matsubara, 2003).

Stress also cause secretion of HCL in the stomach via the stress centres and vagal stimulation (Gannong, 2005).

Symptoms of gastric ulcer includes, abnormal pains, bloating, nausea, loss of appetite, haematemesis, melena, vomiting and loss of weight, (Merck, 2006). The disease is diagnosed with the acid of adenoscopy of barium contrast rays, eosophagogastric duodenoscopy(EGD), urea breath i.e. non invasive direct culture from EGD biopsy,(test and Diagnosis, 2010) store antigen and histological examination. It could be diagnosed differently through gastritis, stomach cancer gastroesophageal reflux disease(GERD) pancrititis, hepatic congestion, cholecystitis, biliary colic, inferior myocardial infarction, pleurisy, pericarditis; (Atlas of pathology, 2007).

Treatment of gastric ulcer involves use of antiulcerogenic drugs, e.g. proton pump inhibitors, omeprazole, H_2. Inhibitors; cimetidine, ranitidine and antacids but Proton pump inhibitors (PPI) are the most potent in ulcer treatment, (Tripathi, 2008).

Electrolyte levels are affected in disease situations and were investigated in the study. Electrolyte ions are needed for the homeostasis balance in the body i.e. the intracellular and extracellular environment and particularly the maintenance of osmotic gradient that regulate PH, hydration, nerve function

through various mechanisms (Estevex, 2008). Basic electrolytes are sodium, calcium, potassium, chloride, bicarbonate, magnesium, hydrogen phosphate (medicine net.com, 2014). Sodium is the major electrolyte in the extracellular fluid normal range 135 – 145 mEq/L. It regulates total amount of water in the body, brain, nervous system, muscles and generate electrical signals for cell to cell communication, (Guyton, 2006). Excess sodium (hypernatraemia) may be caused by hyperosmotic dehydration an inability for the secretion of antidurectic hormone for the conservation of water by the kidneys. But the direct cause is dehydration hypernatraemia is hypertonic, (Anderoll, 1982) and results in hyper osmolality with associated thirst, mental confusion, coma and death particularly from cerebral dehydration. (Dewey, 1989).

Low sodium level, hyponatraemia is the most frequent electrolyte anomaly (Burton, 2000. Tiet 3, 1990.). It may be associated with envolemia or hypovolemia, hypervolemia. Hyponatraemia mainly results from dilution in extracellular fluid (Biswas, 2007). It may also result from burns, severe exudation skin lesion, massive sweating, alimentary secretions, vomiting, diarrhea, fistulae, intestinal obstructions (Dewey, 1989).

Potassium is mainly found in the intracellular fluid compartment. It regulate heartbeat. Increase concentration (Hyperkalaemia) leads to cardiac arrhythmias and hyperkalaemia develops whenever potassium intake exceeds the sum of renal extra potassium losses. Hypokalaemia; low potassium reflect total body reduction with clinical consequences as in low heart beat regulation. Normal values; 3.5 – 5.0MEql. Calcium is needed in muscle contraction, heart functioning, nerve signaling, blood clotting, bone building (Bring Hurst, 2007). High level of calcium; Hypercalaemia lead to depress neuromuscular excitability and cardiac arrhythmias, but at hypocalcemia (reduce calcium there is increase excitability of the nerve and muscle and resultant tetany i.e. spatial skeletal muscle contraction. Normal calcium level is 5MEql.

Magnesium is required as catalyst in the metabolism of carbohydrate its content in extracellular fluid in 1.8 – 2.5MEq/L. value above this leads to depression of the nervous system activities and the muscular contraction. However, low magnesium levels leads to increase irritability of the peripheral vasodilation and nervous system. Bicarbonate ion acts as buffer to maintain the normal level of acidity PH. The normal range of bicarbonate is 22 – 30 mmol/L. this range may be disrupted in kidney, respectively and metabolic anomalies (update .com, 2004). The functional aactivity of bicarbonate is for stomach acid neutralization.

Chloride is mainly extracellular electrolyte, the normal range is 90-108mmol/L while the intracellular value is 44 – 54mmol/L as in erythrocyte. Excess is excreted in urine, loss in sweet regulated by aldosterone. Decreased plasma chloride concentration, hypochloremia is associated with chronic pyelonephritis, vomiting and in metabolic acidosin with hypokalemia. Tilkian, 1975. Tietz, 1987. But increased chloride levels (hyperchloremia) is associated with renal tubular acidosis decrease, CO2 content and hypokalaemia. It occurs with dehydration acute renal failure, metabolic acidosis with prolonged diarrhea and NaHCO3 loss. Other associated factors are high intake of salt and over treatment with saline solution. It is therefore very necessary to assess electrolyte levels in gastric ulcer medication to avoid complications from the drugs aggravating the disease situation and thus streamlining for the effective management of the disease.

MATERIALS AND METHODS

Twenty-four (24) adult male and female albino rats of average weight 100g – 140g were used for the study. The rats were kept in a well-ventilated faculty of pharmacy animal house and fed with pellets and water. The rats were divided into groups.

Grouping Of Animals: The rats were divided into six (6) groups and the drugs administered based on their body weight. Group 1; Control group without ulcer and without treatment, Group 2; induced with ulcer without treatment, Group 3; administered with 0.34mls of gelusil and 2.1ml of sodium bicarbonate and 1.89ml of omeprazole, Group 4; administered with 1.5ml of sodium bicarbonate and 1.89ml of omeprazole, Group 5; administered with 0.28ml of sodium bicarbonate and 1.9ml of omeprazole. Group rats were administered with 1.75ml of omeprazole. The drugs were given orally using 1.0cm canula by-passing the oesophagus and delivered into the stomach, (Ber tram 2004), (Robert etal 1979).

Rats in groups 2, 3, 4, 5 and 6 were starved for 24hrs to exclude feeding as source of acid stimulation for ulcer. Each was given 2.5ml/kg of ethanol.

Blood Collection and Assessment of Ulceration. The rats were anaesthesized with chloroform and 5ml of blood collected by vene puncture, Dacie & Lewis 2007. The blood was spun and plasma analyzed for various electrolytes. Gastric ulcer was assessed by incising the isolated stomach longitudinally. The ulcerated spots indicated ulcer which were very distinct using hand lens.

Electrolyte Determination: This was done using automated electrolyte analyser, VITROSDT 6011, and the various values of the electrolytes obtained.

RESULTS

Sodium: The results showed significant difference in sodium between the six groups (F=3.369, P <0.05), table 1 figure 1. The sodium in group 6 was significantly higher than group 2(p<0.05) and insignificantly higher than groups 1, 2, 3, and 4(P>0.05).

Table 1 Electrolyte/Bicarbonate Levels

Groups	Na	K	Mg	Cl	Ca	HCO_3
1	126.85 ± 1.56	76.36 ± 0.88	1.53 ± 0.05	93.40 ± 2.09	0.018 ± 0.005	15.75 ± 2.25
2	124.03 ± 3.31	87.25 ± 5.41^{a}	1.70 ± 0.08^{a}	91.88 ± 1.71^{a}	0.013 ± 0.010	13.33 ± 0.38
3	125.50 3.31	22.24 ± 8.17^{ab}	1.88± 0.05ab	98.13± 2.99^{b}	0.048± 0.10^{b}	9.33± 0.74^{a}
4	126.43 ± 1.40	48.19 ± 19.40^{abc}	1.48± 0.10^{bc}	93.25± 0.66^{c}	0.010± 0.008^{c}	17.63± 5.16^{b}
5	127.45 ± 1.42^{b}	8.85 ± 3.28^{abd}	1.59± 0.05^{bc}	94.08± 1.47^{c}	1.070± 0.047^{abcd}	10.33± 0.84^{ad}
6	130.83 ± 1.81^{abcd}	8.91 ± 1.87^{ab}	1.57± 0.06^{bc}	90.63± 1.32^{ce}	0.023± 0.058^{e}	13.50± 0.53^{cd}

FIGURE 1:- SHOWING COMPARISON OF SODIUM ELECTROLYTES BETWEEN THE DIFFERENT EXPERIMENTAL GROUPS

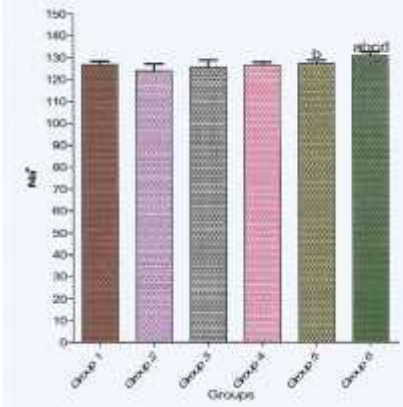


FIGURE 2:- SHOWING COMPARISON OF POTASSIUM ELECTROLYTE BETWEEN THE DIFFERENT EXPERIMENT GROUPS

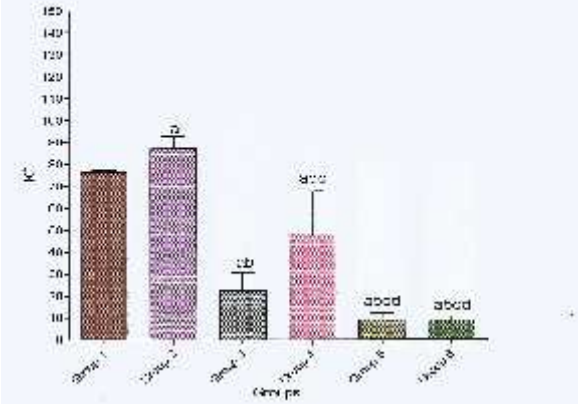


FIGURE 3:- SHOWING COMPARISON OF MAGNESIUM ELECTROLYTE BETWEEN THE DIFFERENT EXPERIMENT GROUPS

Mg2+

Magnesium in group 2 was significantly higher than group 1 ($p<0.05$). Group 3 was significantly higher than group 1 and 2 ($p<0.05$) while that of group 4, 5 and 6 were significantly less than group 2 and group 3 ($p < 0.05$).

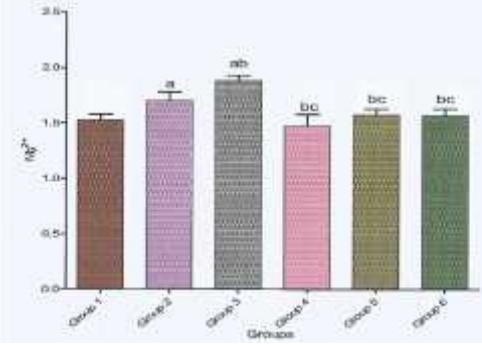


FIGURE 4:- SHOWING COMPARISON OF CHLORIDE ELECTROLYTE BETWEEN THE DIFFERENT EXPERIMENT GROUPS

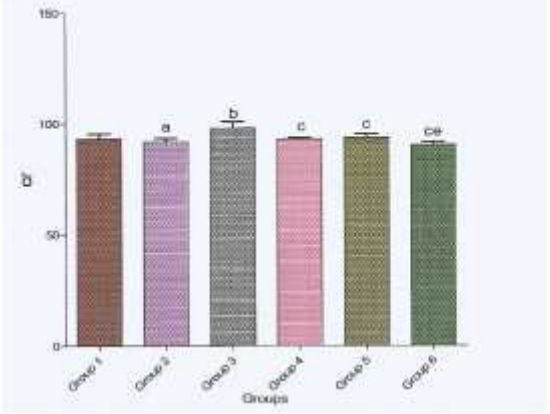


FIGURE 5:- SHOWING COMPARISON OF CALCIUM ELECTROLYTE BETWEEN THE DIFFERENT EXPERIMENT GROUPS

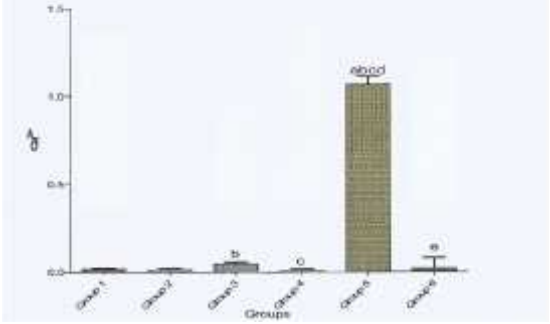
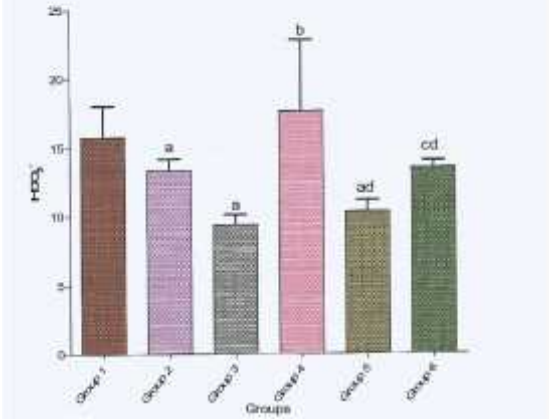


FIGURE 6:- SHOWING COMPARISON OF BICARBONATE ELECTROLYTE BETWEEN THE DIFFERENT EXPERIMENT GROUPS



Potassium: the mean potassium was significantly different between groups (F=51.90, P<0.05), table 1 figure 2. Potassium in group 2 was significantly higher than group 1 (P<0.05). group 3 potassium was significantly less than group 1 and 2 (P<0.05) while potassium in group 4 was significantly less than group 1 and 2 but significantly higher than group 3 (P<0.05). Values of potassium in group 5 and 6 were significantly less than that of group 1, 2, 3, 4 and 5 (P<0.05). There was no significant difference in potassium levels between group 5 and 6 (P<0.05).

Magnesium: Magnesium levels in group 2 was significantly higher than group 1 (P<0.05). in group 3 the magnesium concentration was significantly higher than group 1 and 2 (P<0.05) whereas that of groups 4, 5 and 6 were significantly less than group 3 (P<0.05) , table 1 figure 3.

Chloride: Chloride levels in group 2 were significantly higher than group 1 (P<0.05) while that of group 4, 5 were signinficantly less than group 3 (P<0.05). Group 6 levels were significantly less than those of group 3 and 5; table 1 figure 4.

Calcium: calcium in group 3 was significantly higher than group 2 (P<0.05) but in group 4 was significantly less than

those of group 3 and group 5 was significantly higher than group 1, 2, 3, 4 and 6 (P<0.05); table 1 figure 5.

Bicarbonate: Bicarbonate (HCB) in group 3 was significantly less than that of group 1 (P<0.05) while the value obtained in group 4 was significantly higher than group 2 and that in group 5 was significantly less than group 1 and 4 (P<0.05)

The mean HCO3 in group 6 was significantly higher than group 3 and significantly less than group 4, (P<0.05), Table 1 figure 6.

DISCUSSION

The study had shown variations in the various electrolytes in the different groups of therapy treatment in gastric ulcer. Sodium in group six was higher than those in other groups. Group six rats were treated with omeprazole, it means this drug enhances the concentration of sodium. Increase in sodium hypernatraemia may be as a result of hyperosmotic dehydration i.e. inability of the antidiuretic secretion for conservation of water by kidney. Hypernatraemia may also result due to hyperosmolality with associated thirst, mental confusion, coma and even death (Hardy, 1989). This result has shown the side effects of omeprazole in the treatment of gastric ulcer. However, omeprazole is one of the most potent proton pump inhibitor (PPI) in the treatment of gastric ulcer. Even in groups treated with antacids are highly consumed in minor signs like heartburns meaning they are at risk of hypernatraemia ,these drugs therefore need to be administered with caution, particularly the relationship between high sodium levels and hypertension.

Potassium salt increased significantly in group 2 rats with ulcer without treatment. This means that gastric ulcer has the tendency of increasing potassium levels. This means that in gastric ulcer there is the tendency of developing cardiac arrhythmias (Guyton, 2006). High potassium level; hyperkalaemia occurs when potassium intake exceeds the sum renal extra potassium losses. (Green borg, 2005)Potassium is mainly found in the intracellular fluid compartment. But in group 5 treated with calcium carbonate and omeprazole there was decrease in potassium levels; hypokalaemia. It means that calcium carbonate and omeprazole have the tendency of decreasing potassium levels like hypokalaemia. Hypokalaemia is an indication of low potassium levels in the body, may result in raised blood pressure, abnormal heart rhythm muscle weakness, muscle cramps, tremor and myalgia(Krishna, 1989). Increase in magnesium levels observed in group 2 rats with gastric ulcer without treatments also pointed the distorted of physiology in the disease situation. Group 3 rats with magnesium trisillicate and omeprazole had slightly high levels of potassium than every other group. This may be the effects of potassium triscillicate antacids administration in this group but the effect of gastric ulcer is not ruled out as it has close range results in group 2. High magnesium levels lead to depression of the nervous system and muscular contraction. Significant decrease of magnesium was observed in group 4, 5 and 6 treated with sodium bicarbonate and omeprazole calcium carbonate and that of omeprazole only. Indications from dual effects from antacids and omeprazole are observed because in group 2 with ulcer without treatment had near normal magnesium concentration. This is another confirmation of the deleterious effects of some antacids. Chloride increase was noticed in group 2 with ulcer without treatment, such alevation, hyperchloremia has negative implications, e.g. renal tubular acidosis, decrease CO2 content and hypokalaemia. But low levels of chlorides were observed in groups 4, 5, and 6 indicating that calcium bicarbonate, sodium bicarbonate and magnesium triscillicate have hypochloremic effects in gastric ulcer. Decreased plasma chloride concentration is associated with chronic pyelonephritis vomiting calcium levels were higher in group 5 treated with antacids, calcium carbonate and omeprazole.

It is quite deductive that such increase is therapy dependent. Increased calcium levels; hypercalcaemia leads to depressed muscular excitability and cardiac arrhythmias. However all other groups showed low calcium levels; hypocalcaemia causes increase neuromuscular excitability and resultant tetany, Guyton, 2006.

References

Atlas of pathology, Internet retrieved 2007 Andy (1999) Biswas, M. (2007) Hyponatraemia in clinical practice.

Burton, H (2000) In women in Need. http://www.linkedin.com/pub/hy-burton

Bringhurst, F. R., De May, M. B. and Kronenberg, H. M. (2007) Hormones and disorders of mineral metabolism. In Goldman. L., Ausiello, D. eds. 23rd ed. Philadelphia; Pa Sannders, Elsevier PP 6-2011.

Boekama, P. J. Samson, M, Van Berge Henegonwen, G.P. Smoutt, A. J. P. M(1999) coffee and gastrointestinal function: facts and fiction. A review, *Scandinavian Journal of Gastroenterology* Vol. 34, PP230, 35 – 39.

Looke, S. O., Brown, P. C. and Saunla, Y. J. (1978) Anttacids and side effects in relation to peptic ulcer JCP; 69(9): 483 – 489.

Dacie J. V., Lewis, S. M. (1975): In Practical Haematology. Cerda, J. J. (1994) Churchil, London. In a Revolution in Peptic Ulcer disease patient care.

Dewey C, Downs M. Asm, D (1989) Cerebral Dehydration. *Neuro surgery* 25:173 – 178, 42

Estevex J, Baguero E, R. R. Mora (2008) Anaerobic Performnce when dedydrating with water or commercially available sports drinks during prolonged exercise in the heat. *Applied Physiology, Nutrition and metabolism.* 33(2) 290 – 298.

Evans, K. J., Greenberg A. (2005) Hyperkalaemia . *A review J. intensive care med* 20 (5) 272 – 290

Gannong, W. F. (2005) Review of Medical Physiology 2nd Ed. MC Graw, Hill

Guyton, A. C. Hall J. E. (2006) : In textbook of medical physiology, 11th Edition. Saunders Elsvier.

Hardy, R. M. (1989) Vet Clin North Am Small Anim Pract. 19(2) 231 – 40.

Jimmy, E.O., Odeh, S. O., Adelaiye, A. B. (2013) Hypergastrinaemia and HCL in tea drinking associated gastric ulcer. *Journal of Physiobiochemical and metabolism* 2(2) 2 – 4.

Krishna, G. G, Miller, E, Kapour, S. (1989) increased blood pressure during potassium depletion in normotensive men. *The new England Journal of Medicine* 320 (18): 1177 – 82.

Maa, L. W. P., Wanga, J. Y. C., Chowa Lamb, S. K., Choa, C. H.(2000) The role of polyamines in gastric mucus synthesis inhibited by cigarette smoke or extract. *Gut*. 47:170 – 177.

Maiden, L. P., Harns, A. W., Lai, K. C., Hui, H. M., Lam, S. K.(2002) Lansoprazole for the prevention of recurrence

of ulcer complication from long term low dose aspirin. *New Eng. J. Med*. 347: 1623 – 1624.

Matsubara, S., Shibata, H., Ishikawa, F., Yokko Kura. T, takashashi, M, Sugimura, T, Wakabayashi K.(2003) suppression of helicobacter pylori induced gastritis by green tea extract in mongolean gerbils. *Biochem. Biophys. Res. Comm*. 310, 715 – 719.

Medicine Net.com – Electrolytes Internet.,

Merck Manuals (2006) in.Home health handbook for patients and caregivers, Peptic ulcer. Medicine net.com – electrolyte, 2014

Olubuyide, I.O.(1989) An autopsy survey of peptic ulcer disease at Ibadan. *Central African J. Medicine* 35(10) : 501 – 504.

Oyebola, (2002): In textbook of essential physiology 1st Ed. PPI – 244 Ibadan.

Robert, A.(1979) Cytoprotection by prostaglandins Gastroenterol. 77(4) 761 – 767 Test and diagnosis, retrieved Internet.

Tilkian, C. T. (1975) In clinical implications of labouratory tests 2nd Ed. Pp 30 – 39.

Tietz W. T.(1987): In fundamentals in clinical chemistry 5th Ed. London, W. B. Sannders. pp 301 – 308.

Tripathi K.D. (2008): In essential of Medical Pharmacology. 6th Ed. New Behli.

****