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Original Research Article

Evaluation of Serum Immunoglobins Electrolytes and Membrane Potentials on Pulmonary Tuberculosis Subjects in Owerri, Imo State

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Abstract

The study was carried out to determine the levels of immunoglobulins (IgM, IgE and IgG), electrolyte (sodium, potassium, chloride and bicarbonate) and membrane potential in pulmonary tuberculosis patients attending Awo Omamma General Hospital Imo State. A total of 200 individuals (males and females) comprising 100 newly diagnosed pulmonary tuberculosis patients and control group consisting of 100 apparently healthy individuals of the same age bracket (20 – 60 years). The levels of immunoglobulins was determine by Enzyme linked immunoassay (ELISA) while membrane potential was determined by Nerst equation. Serum electrolyte was determine by standard method. The results showed that sodium and potassium level of tuberculosis subjects (132.25 ±3.61mmol/l and 3.38±0.29mmol/l respectively) were significantly reduced when compared with the control (137.30± 3.07mmol/l and 3.93± 0.27 mmol/l respectively) at P<0.05. Bicarbonate values of the tuberculosis subjects (21.28±2.16 mmol/l) was lower than the control (23.43 ±2.72mmol/l) at p<0.05. Chloride values of the tuberculosis (102.98 ±6.34mmol/l) was higher than that of the control (99.69±4.51mmol/l) and the difference was significant. Sodium and potassium level of female tuberculosis subjects were higher than that of male tuberculosis subject. Bicarbonate and chloride values of the female tuberculosis subjects were lower than the male tuberculosis subjects. The mean calcium of the tuberculosis subjects (8.97±0.33 mg/dl) was lower than the control (9.28 ±0.40mg/dl) and the difference was significant. Membrane potential of the tuberculosis subjects (106.28±5.84mV) was higher than that of the control (118.37±7.26mV) and the difference was significant. IgM, IgE and IgG level of tuberculosis subjects (5.85 ±0.57, 0.96 ±0.16ug/ml and 9.55 ±0.48mg/ml respectively) was higher than that of control subjects (5.51± 0.50ug/ml, 0.52± 0.15ug/ml and 8.84± 0.53ug/ml respectively) and their differences was significant. There was no difference between the sex. Tuberculosis brings about the development of electrolyte imbalances including hyponatremia, hypokalemia, hypochloremia, and hypocarbonemia. There was also increase in immunoglobulins in tuberculosis condition.This could probably indicate that the use of serum immunoglobulins, electrolyte and membrane potentials could be benefitial in diagnosis and management of pulmonary tuberculosis.

Keywords: Immunoglobins, Electrolytes, Membrane Potentials, Pulmonary Tuberculosis

INTRODUCTION

Tuberculosis (TB) is an infectious disease caused by the bacillus *Mycobacterium tuberculosis* (MTB). It is the most dangerous bacterial infection responsible for severe increase in death cases. The Tubercle bacillus was discovered by Robert Koch in 1882. There are several reports indicating that tuberculosis is an age old dreadful disease even from ancient times. The disease was called “consumption” in the past because of the way it would consume from within anyone who became infected (Sharma and Sakar, 2018).

Tuberculosis is a chronic granulomatous infectious disinfection occurs via aerosol, and inhalation of a few droplets containing *M. tuberculosis* bacilli after infection, *M. tuberculosis* pathogenesis occurs in two stages. The first stage is an asymptomatic state that can persist for so many years in the host, called latent TB. (Kaufman, 2014). In the year 1993, World Health Organization (WHO) declared TB a global Public health emergency. About one third of the world’s

population (> 2 billion), are infected with TB bacilli. 10% of the people infected with TB bacilli because sick with active TB in their lifetime (Hachart and Pamda, 2016).

According to WHO report, global population with burden of disease caused by TB from 1990 – 2011 was 6948 million and total number of multi-drug resistant (MDR) cases from 2005- 2011 were 61690 (Harries *et al*., 2016). In 2011, there were an estimated 8.7 million incident cases of TB (range, 8.3 million – 9.0 million) globally. Highest numbers of incidence were reported in Asia (59%) and Africa (26%). Estimates of the burden of TB disease among children have also been carried out. The figures are 4,90,000s cases and 64,000 deaths among HIV – negative children per year (Sharma and Sakar, 2018).

TB is one of the leading causes of death among women 0.5 million woman succumbed to TB. This include 300,000 (range 250,000 – 350,000) TB deaths among HIV negative woman (Kaufinan 2014). Most cases of TB are caused by *M. tuberculosis* and the reservoir of infection is humans with active TB. Most cases of TB are pulmonary and acquired by person to person transmission of air borne droplets of organisms. Oropharyngeal and intestinal TB contracted by drinking dairy milk contaminated with *M. Bovis* rarely seen nowadays and usually in constricts with tuberculosis and unpasteurized milk (Hachart *et al*., 2016).

Furthermore, it is known that immunoglobulins may affect Tuberculosis. Immunoglobulins, also known as antibodies, are glycoprotein molecules produced by plasma cells. They act as a critical part of the immune response by specifically recognizing and binding to particular antigens, such as bacteria or viruses and aiding in their destruction. The antibody immune response is highly complex and exceedingly specific. The various immunoglobulin classes and subclasses (isotypes) differ in their biological feature, structure, target specificity and distribution.

It was found recently that during *Mycobacterium tuberculosis* infection (MTB), increase in calcium influx or release of calcium from intracellular calcium pool activates the intracellular calcium – signaling pathway, thereby activate the gene expression of anti-infection and immune protective proteins in immune cells, especially macrophages (Gupta *et. al*., 2013). This increase in calcium signaling enhances the phagocytic activity and the anti MTB ability of immune cells, ultimately enhancing the anti-MTB ability of the whole Immune system (Gupta *et al*., 2013). As the key player in maintaining the intracellular calcium level, calcium channels have crucial roles in regulating the calcium-signaling pathway (Gupta*et al*., 2013). This in other words affects membrane potential. Membrane potential is the voltage difference between the external and internal cells.

Pulmonary tuberculosis is a bacterial infection due to *Mycobacterium tuberculosis*, spread from person to person through inhalation of infected respiratory droplets. After infection, *M. tuberculosis* multiplies slowly in the lungs and is usually eliminated spontaneously or lies dormant. Only 10% of cases develop active tuberculosis. In certain countries, half of newly diagnosed tuberculosis patients are co-infected with HIV (WHO, 2018). There have been researches on tuberculosis, its clinical manifestation and treatment over the last decades, but there is little or no information regarding pulmonary tuberculosis in relative to immunoglobulin calcium and membrane potential. Hence, the reason for this study.

MATERIALS AND METHODS

Study Area

The study was conducted at the Awo-Omama General Hospital, Oru East. Awo-Omama General Hospital, is a hospital in Oru East LGA of Imo State in Eastern Nigeria and indigenous ethnic group is Igbo. Awo-Omama General Hospital is one of the secondary health institution established in Imo State to provide and facilitate adequate health care to individuals, it provides a training ground for health professionals to be trained and re-train. Also, it promotes and supports research development.

Imo state has an estimated population of 3,927,563, which comprises 1,976,471 male and 1,951,092 female. The city is uprising with the development of new hotels, schools, markets, churches and industries in addition to changes in demographic geography, nutritional and lifestyle.

Study Population

A total of One hundred (200) subjects within the ages twenty and sixty were recruited for this study. One hundred (100) were pulmonary tuberculosis subjects who were newly diagnosed of tuberclosis in Federal Medical Centre Owerri, consisting of 50 males and 50 females. One hundred (100) was apparently healthy individuals who serve as controls subjects of the same age limits and sex who have not record any other ailment.

Sample Collection

Venous blood samples (5ml) were collected asceptically by venipunture from each of the subjects using a 5ml sterile disposable syringe and needle. The whole blood samples were dispensed into a pre -labeled plain dry specimen container

and allowed to clot. The clotted samples were centrifuged at 3000rpm for 10 minues to separate and obtain the serum. The separated serum was used to assay IgM, IgG, IgE and electrolytes.

Laboratory assays

The determination of Serum Immunoglobulin IgM IgG, and IgE was done by ELISA Method (Per and Bo, 1998). While the determination of Sodium, Potassium, Chloride, and Bicarbonate was done by colorimeteric method (Maruna, 1958)

Determination of Calcium was done by the Method of Ochei and Kolhartkar, (2000) while determination of Membrane Potential using Nerst Equation (Franco *et al*., 2016)

Statistical Analysis

Datas were analysed using software statistical package for social sciences (SPSS) version 21.0. The results was expressed as mean and standard deviation (mean $\pm$ SD).Difference in mean values between groups were assessed by Student t-test. Tests with a probability value of $P<0.05$ was considered statistically significant.

RESULTS

Table-1: The Mean ± SD Levels of Serum electrolytes in Pulmonary tuberculosis Subjects and Control Subjects.

Parameters	Pulmonary Tuberclosis Subjects (n-100)	Controls Subjects (n=100)	t-value	p-value
Na+ (mmol//l)	132.25 ±3.61*	137.30 ±3.07	-10.651	0.0001
K+(mmol//l)	3.38 ±0.29*	3.93 ±0.27	-13.752	0.0001
Cl (mmol//l)	102.98 ±6.34*	99.69± 4.51	4.228	0.0001
HCO_3(mmol/l)	21.28 ±2.16*	23.43± 2.72	-6.194	0.001

*: Significantly different from control at $P < 0.05$

Table 1 showed the mean and standard deviation values of the Pulmonary tuberculosis and control subjects. Sodium and potassium level of tuberculosis subjects (132.25 ±3.61mmol/l and 3.38±0.29mmol/l respectively) were significantly reduced when compared with the control (137.30± 3.07mmol/l and 3.93± 0.27 mmol/l respectively) at $P<0.05$. The mean value of bicarbonate of the tuberculosis subjects (21.28±2.16 mmol/l) was lower when compared with control (23.43 ±2.72mmol/l) and the difference was statistically significant at $P<0.05$. Chloride values of the tuberculosis (102.98 ±6.34mmol/l) was higher when compared with the control (99.69±4.51mmol/l) and the difference was statistically significant at $P<0.05$.

Table-2: Mean±SD Values of Serum electrolyte in Male and Female Pulmonary Tuberculosis Subjects.

Parameters	Male-pulmonary Tuberculosis Subjects (n-50)	Female-pulmonary Tuberclosis Subjects (n=50)	t-value	p-value
Na+(mmol/l)	131.56 ±3.74	132.94 ±3.37	-1.937	0.056
K+(mmol/l)	3.35 ±0.31	3.41 ±0.27	-0.933	0.353
Cl(mmol/l)	105.80 ±5.98*	100.16 ±5.41	4.945	0.0001
HCO_3	21.56 ±2.36	21.00 ±1.92	1.303	0.196

*: Statistically significant when compared with female pulmonary tuberculosis at $P < 0.05$

Table 2 shows the mean ± standard deviation of serum electrolytes in male and female pulmonary tuberculosis subjects. Result from table 2 shows that sodium and potassium level of female tuberculosis subjects (132.94 ±3.37mmol/l and 3.41±0.27mmol/l respectively) were higher when compared with male tuberculosis subjects (131.56± 3.74mmol/l and 3.35± 0.31 mmol/l respectively) and were not statistically significant at $P>0.05$. Bicarbonate values of the female tuberculosis subjects (21.00±1.92 mmol/l) was lower when compared with the male tuberculosis subjects (21.56 ±2.36mmol/l) and the difference was not statistically significant at $P>0.05$. Chloride values of female tuberculosis subject (100.16 ±5.41mmol/l) was lower when compared with the male tuberculosis subjects (105.80±5.98mmol/l) and the difference was statistically significant at $P>0.05$.

Table-3: Mean ±SD Values of Serum calcium and membrane potential in Pulmonary tuberculosis Subjects of the Study Population.

Parameters	Pulmonary tuberculosis Subjects (n-100)	Controls Subjects (n=100)	t-value	p-value
Serum Calcium(mg/dl)	8.97± 0.33*	9.28 ±0.40	5.942	0.0001
Redcell Calcium (mg/dl)	4.22± 0.16*	3.92± 0.12	4.820	0.001
Membrane potential (mV)	106.28 ± 5.84*	118.37± 7.26	5.450	0.01

Key:
*:statistically significant (P<0.05)

Table 3 shows the mean ± standard deviation of calcium and memebrane potential in pulmonary tuberculosis subject. The mean calcium of the tuberculosis subjects (8.97±0.33 mg/dl) was lower when compared with the control (9.28 ±0.40mg/dl) and the difference was statistically significant at P<0.05. Membrane potential of the tuberculosis subjects (106.28 ± 5.84mV) was higher when compared with the control (118.37± 7.26mV) and the difference was statistically significant at P<0.05.

Table-4: Mean±SD values of Serum calcium and membrane potential in Male and Female Pulmonary Tuberculosis Subjects.

Parameters	Male-pulmonary tuberculosis Subjects (n-50)	Female-pulmonary Tuberclosis Subjects (n=50)	t-value	p-value
Serum Calcium(mg/dl)	8.99 ± 0.34	8.96 ±0.32	0.420	0.676
Red cell Calcium (mg/dl)	4.20 ±0.26	4.06 ±0.12	0.742	0.553
Membrane potential(mV)	107 ±7.48	110± 9.31	1.096	0.520

Table 4 shows the mean ± standard deviation of serum calcium and membrane potential in male and female pulmonary tuberculosis subjects. The mean calcium of the female tuberculosis subjects (8.96±0.32 mg/dl) was lower when compared with the male tuberculosis subject (8.99 ±0.34mg/dl) and the difference was not statistically significant at P>0.05. Membrane potential of the female tuberculosis subjects (110± 9.31mV) was lower when compared with the male tuberculosis subject (107 ±7.48 mV) and the difference was not statistically significant at P>0.05.

Table-5: Mean ±SD Values of Serum Immunoglobulins (IgM, IgG and IgE) in Pulmonary Tuberculosis Subjects of the Study Population

Parameters	Pulmonary tuberculosis Subjects (n-100)	Controls Subjects (n=100)	t-value	p-value (0.05)
IgM(µg/ml)	5.85 ±0.57*	5.51± 0.50	4.487	0.001
IgE(µg/ml)	0.69 ±0.16*	0.52± 0.15	8.230	0.0001
IgG(mg/ml)	9.55± 0.48*	8.84 ±0.53	9.962	0.0001

*: Statistically significant from control at P<0**.05**

Table 5 above shows the mean and standard deviation values of the Tuberculosis subject and control subjects. IgM level of tuberculosis subjects (5.85 ±0.57ug/ml) was higher when compared with the control subjects (5.51± 0.50ug/ml) and the difference was statistically significant at P<0.05. IgE level of tuberculosis subjects (0.96 ±0.16ug/ml) was higher when compared with the control subjects (0.52± 0.15ug/ml) and the difference was statistically significant at P<0.05. IgG level of tuberculosis subjects (9.55 ±0.48mg/ml) was higher when compared with the control subjects (8.84± 0.53ug/ml) and the difference was statistically significant at P<0.05.

Table-6: Mean±SD values of Serum IgM, IgE and IgG in Male and Female Pulmonary Tuberculosis Subjects.

Parameters	Male-pulmonary tuberculosis Subjects (n-50)	Female-pulmonary Tuberclosis Subjects (n=50)	t-value	p-value (0.05)
IgM (µg/ml)	5.88 ±0.57	5.81 ±0.58	0.662	0.509
1gE(µg/ml)	0.69± 0.16	0.69 ±0.15	0.064	0.949
IgG(mg/ml	9.53 ±0.45	9.57 ±0.50	-0.377	0.707

Table 6 above shows the mean and standard deviation values of the male Tuberculosis subject and female tuberculosis subjects. IgM level of female tuberculosis subjects (5.81 ±0.58ug/ml) was lower when compared with male tuberculosis subjects (5.88± 0.57ug/ml) and the difference was not statistically significant at P>0.05. IgE level of female tuberculosis subjects (0.69±0.15ug/ml) was equivalent to that of male tuberculosis subjects (0.69± 0.16ug/ml) and the difference was not statistically significant at P>0.05. IgG level of female tuberculosis subjects (9.57 ±0.50mg/ml) was higher when compared with the male tuberculosis subjects (9.53± 0.45mg/ml) and the difference was not statistically significant at P>0.05.

DISCUSSION

Electrolyte disturbances are common in patients with pulmonary tuberculosis. In this study, it was observed that sodium level of pulmonary tuberculosis subjects was significantly lower than that of the control. This decrease level of sodium (Na^+) found in TB infected subjects when compared with the control subject, is consistent with previous study (Olalekan *et al*., 2015). This could be as a result of increase in serum osmolality, resulting in movement of water out of the cells and subsequently in a reduction of serum sodium ion levels by dilution. This can be attributed to the loss of Na+ through diarrhea. Uncontrolled pulmonary tuberculosis can also induced hyponatremia due to osmotic dieresis. Hyponatremia can occur as a syndrome of inappropriate antidiuretic hormone secretion (Goli *et al*., 2016).

Similarly, the level of potassium was significantly lower in pulmonary tuberculosis patients when compared to the control patients. This agreed with the work of Kaur *et al*., (2021) in which potassium could be associated with gastrointestinal loss of potassium ion due to malabsorption syndromes (vomiting and diarrhoea) and renal loss of potassium ion due to osmotic dieresis (Yang and Palmer, 2010). In the stress situation due to severe/chronic illness there is increased catabolism of protein leading to the movement of potassium ion from the intercellular compartment to the plasma and consequently excreted in the urine, sweat and vomitus without any compensatory replacement through food due to anorexia a common feature of pulmonary tuberculosis (Ganiger *et al*., 2019). The mean value of chloride gave the same pattern as the level of Na+ in the patients because sodium is always in association with chloride in most cases, therefore the same reason for the level of Na+ in the patients also holds for this. The lower significant bicarbonate level in the pulmonary tuberculosis patients than the normal patients can be attributed to the body's compensatory mechanism to maintain electrochemical neutrality due to the plasma levels of Na+ and chloride.

The level of Calcium concentration in the pulmonary tuberculosis infected patients were observed to be lower than the control individual; while the membrane potential was higher than control. These findings were in line with the works of Hendy and El-Nagger (2019), when they reported that the mean serum calcium concentration in pulmonary tuberculosis patients were lower resulting in a higher prevalence of hypocalcaemia in pulmonary tuberculosis patients compared with controls. Thus, it was concluded that this seems to be caused by vitamin D deficiency. Many factors might cause vitamin D deficiency in tuberculosis and resulting hypocalcemia, including decreased dietary intake, decreased outdoor activity and sun exposure, elevated metabolism by steroids, lack of adequate parathyroid hormone secretion, decreased activation owing to kidney dysfunction, and decreased storage in muscles or fat resulting from wasting. There was no significant difference in the mean electrolytes and membrane potential levels between the two sexes in the tuberculosis subjects.

On the other hand, it was observed that the values of IgG, IgM, IgE were found to be significantly increased in tuberculosis patients when compared with control subjects. This significant increase of mean serum IgG, IgM and IgE levels in the tuberculosis patient, is in conformity with some other reports (Naqash and Bhat, 2016; Rohini and Mahesh, 2012). This is due to humoral immune response to antigens invading the body.

Mycobacterium tuberculosis comprises various antigenic components and the fractional estimation demonstrates only a fraction of the total humoral response. Instead, estimation of the total serum IgG, IgE and IGM gives a true reflection of the humural response and therefore, the antigenic load in tuberculosis. It was observed that there was no significant difference in the mean immunoglobulin levels between the two sexes in the patient group. This is in agreement with the work of Naqash and Bhat (2016).

The result of this study have indicated that immunoglobulins, electrolyte and membrane potential are significantly reduced in pulmonary tuberculosis patients which may be associated with high levels of free radicals, oxidative stress and sodium potassium pump malfunction. This could imply that the use of immunoglobulins, electrolyte and membrane potentials could be crucial in diagnosis and management of pulmonary tuberculosis.

APPENDIX I
RAW RESULTS

Electrolyte, Membrane Potential and Immunoglobulins of Pulmonary Tuberculous Subjects

S/N	Sex	Sodium (mmol/L)	Potassium (mmol/L)	Chloride (mmol/L)	Bicarbonate (mmol/L)	Calcium (mg/dl)	IgM (ug/ml)	IgG (ug/ml)	IgE (ug/ml)
1	M	136	3.2	110	24	8.2	6.2	9.2	0.5
2	M	130	3.8	108	22	9.0	5.4	9.9	0.9
3	M	132	3.5	104	18	8.8	5.2	9.1	0.9
4	M	128	3.4	112	18	9.5	5.2	9.1	0.6
5	M	136	3.1	114	20	9.5	6.6	10.2	0.6
6	M	139	3.6	106	25	8.6	7.0	8.9	0.8
7	M	124	3.1	108	25	8.2	5.4	9.4	0.9
8	M	130	3.2	116	22	9.4	5.8	9.4	0.9
9	M	128	3.4	108	21	9.0	5.8	10.1	0.6
10	M	132	3.0	112	19	9.0	6.0	10.5	0.5
11	M	136	2.9	113	19	8.8	6.0	8.7	0.7
12	M	130	3.7	118	22	9.4	6.5	9.3	0.7
13	M	126	3.2	106	26	9.4	6.2	9.0	0.6
14	M	134	3.0	106	25	8.5	6.2	9.2	0.7
15	M	130	3.5	104	21	8.5	6.0	9.0	0.9
16	M	132	3.4	112	25	9.6	6.5	9.0	1.1
17	M	136	3.9	108	24	9.0	5.4	10.4	0.9
18	M	128	3.2	102	19	9.2	5.5	10.2	0.5
19	M	129	3.4	118	20	9.2	5.2	9.6	0.4
20	M	127	3.2	112	18	8.9	5.2	9.0	0.9
21	M	130	3.0	108	26	9.1	5.5	9.4	0.9
22	M	125	3.4	106	24	9.1	6.0	9.5	0.5
23	M	134	3.6	115	21	8.9	6.4	9.2	0.5
24	M	132	3.2	113	19	9.6	6.1	9.2	0.8
25	M	127	3.0	109	22	9.0	6.1	10.1	0.6
26	M	131	3.1	109	23	9.2	7.1	9.1	0.6
27	M	126	2.8	105	23	9.2	5.4	9.5	0.7
28	M	134	3.0	106	24	8.4	5.0	9.6	0.7
29	M	128	3.1	104	26	8.4	5.2	9.4	0.8
30	M	126	3.5	109	22	9.1	5.2	10.2	0.8
31	M	129	3.2	102	19	9.1	5.5	10.1	0.7
32	M	129	3.4	104	20	9.0	6.0	9.4	0.7
33	M	130	3.4	104	20	9.0	6.1	9.4	0.7
34	M	134	3.2	100	22	8.6	6.1	9.6	0.8
35	M	131	3.0	98	20	8.8	6.4	9.6	0.8
36	M	131	3.0	96	18	8.8	6.2	10.2	0.7
37	M	140	3.9	101	19	9.0	6.0	10.0	0.7
38	M	132	4.2	101	23	9.2	7.1	9.4	0.5
39	M	136	3.3	100	20	9.2	5.5	9.1	0.6
40	M	135	3.3	105	20	9.0	5.2	10.2	0.6
41	M	135	3.5	102	19	9.4	5.0	10.0	0.5
42	M	136	3.5	105	20	9.0	6.1	10.0	0.8
43	M	132	3.7	102	21	9.0	5.0	9.4	0.6
44	M	132	3.2	89	24	8.9	5.0	9.6	0.6
45	M	130	3.4	96	22	9.1	6.4	9.2	0.8
46	M	130	3.4	99	22	9.1	6.4	9.0	0.5
47	M	136	3.9	99	20	8.4	6.5	9.7	0.5
48	M	138	4.0	102	20	8.7	6.0	9.2	0.8
49	M	132	3.2	104	22	8.9	6.2	9.5	0.8
50	M	134	3.6	100	24	9.4	6.2	9.5	0.4
51	F	136	3.6	102	20	9.7	5.7	10.2	0.6

52	F	138	3.4	102	20	8.5	5.0	8.4	0.6
53	F	132	3.4	106	24	8.7	6.2	9.7	0.8
54	F	132	3.2	99	24	9.2	6.2	9.2	0.8
55	F	129	3.3	95	20	9.2	5.5	9.2	0.6
56	F	129	3.4	96	19	8.7	5.2	10.5	0.6
57	F	132	3.4	95	19	8.7	5.2	10.2	1.1
58	F	132	3.6	97	22	9.0	6.0	10.2	0.5
59	F	139	3.6	97	20	9.0	6.1	9.6	0.5
60	F	133	3.4	102	18	9.4	6.4	9.6	0.7
61	F	134	3.4	98	18	9.2	5.2	10.0	0.7
62	F	135	3.5	95	21	9.2	5.6	10.2	0.4
63	F	132	3.3	90	20	8.9	6.4	10.2	0.6
64	F	132	3.3	92	21	8.7	6.6	9.4	0.6
65	F	138	3.7	92	21	9.2	5.4	9.4	1.0
66	F	138	3.5	101	19	9.2	5.0	8.9	1.0
67	F	132	3.6	103	19	8.4	5.3	8.6	0.7
68	F	132	3.7	90	20	8.6	6.1	9.2	0.6
69	F	134	3.3	86	22	9.0	6.4	8.4	0.6
70	F	136	3.4	110	20	8.4	5.0	10.4	1.0
71	F	127	3.0	109	22	9.0	5.2	9.0	0.9
72	F	131	3.1	109	23	9.2	5.5	9.4	0.9
73	F	126	2.8	105	23	9.2	6.0	9.5	0.5
74	F	134	3.0	106	24	8.4	6.4	9.2	0.5
75	F	128	3.1	104	26	8.4	6.1	9.2	0.8
76	F	126	3.5	109	22	9.1	6.1	10.1	0.6
77	F	129	3.2	102	19	9.1	7.1	9.1	0.6
78	F	129	3.4	104	20	9.0	5.4	9.5	0.7
79	F	130	3.4	104	20	9.0	5.0	9.6	0.7
80	F	134	3.2	100	22	8.6	5.2	9.4	0.8
81	F	131	3.0	98	20	8.8	5.2	10.2	0.8
82	F	131	3.0	96	18	8.8	5.5	10.1	0.7
83	F	140	3.9	101	19	9.0	6.0	9.4	0.7
84	F	132	4.2	101	23	9.2	6.1	9.4	0.7
85	F	136	3.3	100	20	9.2	6.1	9.6	0.8
86	F	135	3.3	105	20	9.0	6.4	9.6	0.8
87	F	135	3.5	102	19	9.4	6.2	10.2	0.7
88	F	136	3.5	105	20	9.0	6.0	10.0	0.7
89	F	132	3.7	102	21	9.0	7.1	9.4	0.5
90	F	132	3.2	89	24	8.9	5.5	9.1	0.6
91	F	130	3.4	96	22	9.1	5.2	10.2	0.6
92	F	130	3.4	99	22	9.1	5.0	10.0	0.5
93	F	136	3.9	99	20	8.4	6.1	10.0	0.8
94	F	138	4.0	102	20	8.7	5.0	9.4	0.6
95	F	132	3.2	104	22	8.9	5.0	9.6	0.6
96	F	134	3.6	100	24	9.4	6.4	9.2	0.8
97	F	136	3.6	102	20	9.7	6.4	9.0	0.5
98	F	138	3.4	102	20	8.5	6.5	9.7	0.5
99	F	132	3.4	106	24	8.7	6.0	9.2	0.8
100	F	132	3.2	99	24	9.2	6.2	9.5	0.8

Electrolyte, Membrane Potential And Immunoglobulins Of Control Subjects

S/N	Sex	Sodium (mmol/L)	Potassium (mmol/L)	Chloride (mmol/L)	Bicarbonate (mmol/L)	Calcium (mg/dl)	IgM	IgG	IgE
1	M	136	3.7	99	25	9.0	5.4	8.2	0.8
2	M	134	4.0	102	24	9.3	5.7	9.0	0.5
3	M	140	4.5	104	24	9.0	6.2	8.6	0.6
4	M	139	4.0	98	26	9.5	5.4	8.8	0.5
5	M	136	3.9	98	24	8.9	5.0	9.4	0.7
6	M	142	3.9	105	26	8.9	5.1	9.8	0.4
7	M	137	4.2	96	23	9.2	5.1	9.2	0.4
8	M	138	3.8	99	25	9.4	6.2	8.2	0.4

9	M	136	4.4	100	27	9.4	6.0	8.4	0.6
10	M	136	3.9	105	23	9.0	4.5	8.0	0.6
11	M	142	4.1	100	26	9.0	4.2	9.5	0.5
12	M	140	4.2	104	26	9.6	5.6	8.6	0.4
13	M	138	4.0	104	28	9.0	5.5	9.4	0.4
14	M	142	3.8	102	27	8.6	5.2	9.4	0.2
15	M	138	4.6	104	26	8.4	5.2	8.2	0.8
16	M	144	4.0	100	26	8.5	6.2	8.4	0.6
17	M	140	3.8	98	25	9.4	6.0	8.3	0.6
18	M	138	3.8	101	26	10.2	6.0	8.4	0.5
19	M	135	4.2	102	26	9.8	4.9	8.0	0.5
20	M	145	4.5	102	24	9.4	5.2	9.3	0.5
21	M	136	3.9	98	24	9.4	5.7	9.5	0.4
22	M	140	4.2	104	27	10.4	5.1	9.0	0.4
23	M	146	4.5	99	29	9.2	5.1	9.3	0.6
24	M	136	3.9	99	29	9.0	5.4	9.5	0.6
25	M	139	3.6	100	25	9.0	5.5	8.3	0.7
26	M	135	3.8	102	24	9.4	5.2	8.0	0.4
27	M	137	4.4	102	24	9.0	5.2	8.2	0.4
28	M	138	4.2	105	26	9.2	5.4	9.3	0.5
29	M	142	4.0	98	25	9.2	6.0	8.9	0.6
30	M	138	3.8	103	27	9.0	5.0	9.3	0.5
31	M	134	3.8	99	22	9.4	6.2	9.0	0.2
32	M	132	4.0	99	20	9.4	6.1	9.1	0.4
33	M	136	4	102	22	8.9	5.6	9.5	0.4
34	M	134	3.9	104	24	9.6	5.5	8.6	0.5
35	M	137	3.8	98	24	9.4	5.2	8.9	0.3
36	M	138	4.1	84	20	9.0	5.4	8.7	0.5
37	M	134	4.1	88	19	9.0	5.4	9.4	0.7
38	M	136	3.9	92	19	9.8	6.3	9.2	0.5
39	M	138	3.7	96	24	9.1	5.1	9.2	0.5
40	M	142	3.7	101	24	9.1	5.1	9.1	0.3
41	M	136	4.0	101	21	9.4	6.0	8.3	0.3
42	M	136	3.9	96	23	9.6	6.2	8.6	0.6
43	M	137	4.2	96	23	9.6	5.1	8.9	0.6
44	M	134	3.6	92	21	8.9	5.4	8.0	0.8
45	M	135	3.6	96	22	9.2	6.3	9.2	0.5
46	M	135	3.4	103	26	9.4	5.5	9.2	0.4
47	M	137	3.5	105	25	9.4	6.2	9.2	0.6
48	M	138	3.5	102	22	8.7	6.4	8.3	0.4
49	M	134	3.6	100	20	10.2	6.1	9.0	0.4
50	M	132	3.4	98	20	10.0	6.1	8.4	0.4
51	F	137	4.0	98	25	10.0	5.2	8.4	0.6
52	F	138	4.0	97	21	9.2	5.5	9.6	0.7
53	F	139	3.8	102	19	9.2	5.0	9.2	0.7
54	F	135	3.8	102	19	9.0	5.0	9.2	0.5
55	F	135	3.6	107	21	9.1	6.2	8.3	0.5
56	F	135	3.9	104	21	9.5	6.2	8.2	0.6
57	F	136	3.5	104	20	9.0	5.4	9.0	0.4
58	F	135	3.7	105	24	9.4	5.0	9.0	0.4
59	F	140	3.9	104	24	9.1	5.2	7.4	0.6
60	F	138	3.9	102	21	9.1	5.1	9.3	0.6
61	F	138	3.4	102	21	9.4	5.0	8.0	0.8
62	F	135	3.5	100	20	9.4	6.2	9.0	0.8
63	F	134	3.7	98	19	9.0	6.2	8.2	0.5
64	F	134	3.8	85	19	9.2	6.0	9.4	1.0
65	F	138	3.9	98	20	9.2	5.4	9.4	0.5
66	F	137	4.0	99	19	9.2	5.4	9.3	0.7
67	F	135	4.2	101	20	9.6	5.0	8.0	0.5
68	F	132	3.9	103	20	9.6	6.5	8.7	0.6
69	F	134	3.6	105	21	8.7	5.4	8.3	0.4

70	F	136	3.6	103	22	10.0	5.3	9.4	0.6
71	F	138	4.6	104	26	8.4	4.5	8.0	0.6
72	F	144	4.0	100	26	8.5	4.2	9.5	0.5
73	F	140	3.8	98	25	9.4	5.6	8.6	0.4
74	F	138	3.8	101	26	10.2	5.5	9.4	0.4
75	F	135	4.2	102	26	9.8	5.2	9.4	0.2
76	F	145	4.5	102	24	9.4	5.2	8.2	0.8
77	F	136	3.9	98	24	9.4	6.2	8.4	0.6
78	F	140	4.2	104	27	10.4	6.0	8.3	0.6
79	F	146	4.5	99	29	9.2	6.0	8.4	0.5
80	F	136	3.9	99	29	9.0	4.9	8.0	0.5
81	F	139	3.6	100	25	9.0	5.2	9.3	0.5
82	F	135	3.8	102	24	9.4	5.7	9.5	0.4
83	F	137	4.4	102	24	9.0	5.1	9.0	0.4
84	F	138	4.2	105	26	9.2	5.1	9.3	0.6
85	F	142	4.0	98	25	9.2	5.4	9.5	0.6
86	F	138	3.8	103	27	9.0	5.5	8.3	0.7
87	F	134	3.8	99	22	9.4	5.2	8.0	0.4
88	F	132	4.0	99	20	9.4	5.2	8.2	0.4
89	F	136	4	102	22	8.9	5.4	9.3	0.5
90	F	134	3.9	104	24	9.6	6.0	8.9	0.6
91	F	137	3.8	98	24	9.4	5.0	9.3	0.5
92	F	138	4.1	84	20	9.0	6.2	9.0	0.2
93	F	134	4.1	88	19	9.0	6.1	9.1	0.4
94	F	136	3.9	92	19	9.8	5.6	9.5	0.4
95	F	138	3.7	96	24	9.1	5.5	8.6	0.5
96	F	142	3.7	101	24	9.1	5.2	8.9	0.3
97	F	136	4.0	101	21	9.4	5.4	8.7	0.5
98	F	136	3.9	96	23	9.6	5.4	9.4	0.7
99	F	137	4.2	96	23	9.6	6.3	9.2	0.5
100	F	134	3.6	92	21	8.9	5.1	9.2	0.5

APPENDIX II

STATISTICAL METHOD AND TERMS

SPSS (Statistical Package for Social Sciences) version 20.0 window software computer programme was used to evaluate the results. The results include standard deviation and Mean. With this computer package, independent student t-test was used to compare for any statistical mean difference between the two groups. This also gives the P value which indicates any difference in the comparism.

Confidence interval = 95%

Level of significance = 0.05

Hypothesis

This is a two tailed test hypothesis**.** Therefore,

Null hypothesis Ho : $x_1 = x_2$

Alternate hypothesis HI : $x_1 \neq x_2$

At 0.05 significant level, the Ho is rejected if the calculated Test statistics (t-test) value $t < -t_{\alpha/2}$ or $t > +t_{\alpha/2}$ otherwise Ho is accepted.

Where, t is the calculated test statistic and $t_{\alpha/2}$ is the computed test statistics from standard statistical table.

REFERENCES

1. Abebe F, Belay M, Legesse M, Ottenhoff T.M, (2018). IgA and IgG against Mycobacterium tuberculosis Rv2031 discriminate between pulmonary tuberculosis patients, Mycobacterium tuberculosis-infected and non-infected individuals. Plos ONE. 13 (19): 4 – 10.
2. Abel L, Fellay J, Haas DW, Schurr E, Srikrishna G, Urbanowski M, (2018). Genetics of human susceptibility to active and latent tuberculosis: present knowledge and future perspectives. Lancet Infectious Disease.18:e64–e75.
3. Achkar J.M, Jenny-Avital E.R, (2011). Incipient and subclinical tuberculosis: defining early disease states in the context of host immune response. Journal of Infectious Disease; 204(Suppl 4):S1179–86.
4. Ahmed N, Hasnain S.E, (2011). Molecular epidemiology of tuberculosis in India: moving forward with a systems biology approach. Tuberculosis. **91** (5): 407–13.

5. Ashenafi S., Aderaye G., Bekele A., Zewdie M., Aseffa G., Hoang A.T.N., Carow B., Habtamu M., Wijkander M., Rottenberg M., Aseffa A., Andersson J., Svensson M., Brighenti S, (2014). Progression of clinical tuberculosis is associated with a Th2 immune response signature in combination with elevated levels of SOCS3. Clinical Immunology; 15: 20 – 25.
6. Bento J, Silva A.S, Rodrigues F, Duarte R, (2011). Diagnostic tools in tuberculosis. Acta Medica Portuguesa. **24** (1): 145–54.
7. Bibbins-Domingo K, Grossman D.C, Curry S.J, Bauman L, Davidson K.W, Epling J.W, (2016). "Screening for Latent Tuberculosis Infection in Adults: US Preventive Services Task Force Recommendation Statement". Journal of American Medical Association. **316** (9): 962–9.
8. Bothamley G.H.(2014) Epitope-specific antibody levels in tuberculosis: biomarkers of protection, disease, and response to treatment. Front Immunol. ;5
9. Boes M, (2010). Role of natural and immune IgM antibodies in immune responses. Molecular Immunology; 37:1141–1149.
10. Bozzano F, Marras F, De Maria A (2014). Immunology of tuberculosis. Mediterranean Journal of Hematology and Infectious Diseases. **6** (1): e2014027.
11. Cai Y, Yang Q, Tang Y, Zhang M, Liu H, Zhang G, (2014). Increased complement C1q level marks active disease in human tuberculosis. Plos ONE. 9:92340.
12. Cambier C.J., Falkow S., Ramakrishnan L, (2014). Host evasion and exploitation schemes of Mycobacterium tuberculosis. Cell; 159:1497–1509
13. Casadevall A (2016). To be or not be a (functional) antibody against TB. Cell; 167:306–307.
14. Cavacini L.A, Kuhrt D, Duval M, Mayer K, and Posner M, (2013). Binding and neutralization activity of IgG1 and IgG3 from serum of HIV infected individuals. AIDS Research & Human Retroviruses; 19:785–792.
15. Centers for Disease Control and Prevention (2011), Core Curriculum on Tuberculosis: What the Clinician Should Know" (PDF) (5th ed) Division of Tuberculosis Elimination. p. 24.
16. Chang T.W, Wu P.C, Hsu C.L, and Hung A.F, (2017). Anti-IgE antibodies for the treatment of IgE-mediated allergic diseases. Journal of Immunology; 93:63–119.
17. Chen J, Zhang R, Wang J, Liu L, Zheng Y, Shen Y, (2011). Interferon-gamma release assays for the diagnosis of active tuberculosis in HIV-infected patients: a systematic review and meta-analysis". Plos One. **6** (11)
18. Chen T, Blanc C, Eder A.Z, Prados-Rosales R, Souza A.C, Kim R.S, (2016). Association of human antibodies to Arabinomannan with enhanced mycobacterial opsonophagocytosis and intracellular growth reduction. Journal of Infectious Disease; 214:300–10.
19. Chin S.T., Ignatius J., Suraiya S., Tye G.J., Sarmiento M.E., Acosta A., Norazmi M.N., Lim T.S (2014). Comparative study of IgA vh3 gene usage in healthy tst- and tst+ population exposed to tuberculosis: deep sequencing analysis. Immunology;144 (6): 124-131.
20. Comas I., Chakravartti J., Small P.M., Galagan J., Niemann S., Kremer K., Ernst J.D., Gagneux S(2010). Human T cell epitopes of Mycobacterium tuberculosis are evolutionarily hyperconserved. National Genetics;42:498–503.
21. Cordero R.J.B., Pontes B., Frases S., Nakouzi A.S., Nimrichter L., Marcio L., Viana N.B., Casadevall A., Rodrigues M.L (2013). Antibody binding to Cryptococcus neoformans impairs budding by altering capsular mechanical properties. Journal of Immunology; 190:317–323
22. Corthesy B, (2017). Roundtrip ticket for secretory IgA: role in mucosal homeostasis? Journal of Immunology; 178:27–32.
23. Cottle L.E (2011). Mendelian susceptibility to mycobacterial disease. Clinical Genetics; 79:17–22.
24. Crowley L.V, (2010). An introduction to human disease: pathology and pathophysiology correlations (8th ed.). p. 374. ISBN 978-0-7637-6591-0.
25. Deng J., Bi L., Zhou L., Guo S., Fleming J., Jiang H., Zhou Y., Gu J.J., Zhong Q., Wang Z., Zhang H., Gu J., Wu F., Zhang Z., Wang D., Hang H., Li Y., Cheng L., He X., Tao S., Zhang X, (2014). Mycobacterium Tuberculosis proteome microarray for global studies of protein function and immunogenicity. Cell Rep.; 9:2317–2329.
26. Doğru D., Kiper N., Özçelik U., Yalçin E., Tezcan I, (2010). Tuberculosis in children with congenital immunodeficiency syndromes. Tuberk Toraks. ; 58:59–63.
27. Encinales L., Zuñiga J., Granados-Montiel J., Yunis M., Granados J., Almeciga I., Clavijo O., Awad C., Collazos V., Vargas-Rojas M.I (2010). Humoral immunity in tuberculin skin test anergy and its role in high-risk persons exposed to active tuberculosis. Molecular Immunology ;47:1066–1073
28. Erb K.J (2007). "Helminths, allergic disorders and IgE-mediated immune responses: where do we stand?". European Journal of Immunology. **37** (5): 1170–3
29. Feng L., Li L., Liu Y., Qiao D., Li Q., Fu X., Wang H., Lao S., Wu C (2011). B lymphocytes that migrate to tuberculous pleural fluid via the SDF-1/CXCR4 axis actively respond to antigens specific for Mycobacterium tuberculosis. European Journal of Immunology; 41:3261–3269.
30. Feris E.J., Encinales L., Awad C., Stern J.N.H., Tabansky I., Jimenez-Alvarez L., Ramírez-Martínez G., Cruz-Lagunas A., Bobadilla K., Márquez E., Granados-Montiel J., Rodriguez-Reyna T.S., Fernandez-Vina M., Granados

J., Zuñiga J., Yunis E.J (2015). High levels of anti-tuberculin (IgG) antibodies correlate with the blocking of T-cell proliferation in individuals with high exposure to Mycobacterium tuberculosis. International Journal of Infectious Disease;43:21–24
31. Fletcher H.A., Snowden M.A., Landry B., Rida W., Satti I., Harris S.A., Matsumiya M., Penn-Nicholson A., Nemes E., Hatheril M., Hussey G., Mahomed H., Tameris M., McClain J.B., Evans T.G., Hanekom W.A., Scriba T.J., McShane H (2016). T-cell activation is an immune correlate of risk in BCG vaccinated infants. National Commun; 7:11290.
32. Fu Y.R., Yi Z.J., Guan S.Z., Zhang S.Y., Li M (2012). Proteomic analysis of sputum in patients with active pulmonary tuberculosis. Clinical Microbiology Infection ;18:1241–124
33. Furth, R.; Schuit, H. R.; Hijmans, W. (2005). "The immunological development of the human fetus". Journal of Experimental Medicine. **122** (6): 1173–88.
34. Ganiger A, Patil L, Mrudula N, (2019). Evaluation of Serum Electrolyte Status among Normal Healthy Individuals and Newly Diagnosed Cases of Pulmonary TB in Tertiary Care Hospital in Bidar: An Observational Study. Indian Journal of Medical Biochemistry; 23(3):316–319.
35. Geisberger R, Lamers M, and Achatz G, (2016). The riddle of the dual expression of IgM and IgD. Immunology; 118:429–437.
36. Gill J, Prasad V, (2019). "Testing Healthcare Workers for Latent Tuberculosis: Is It Evidence Based, Bio-Plausible, Both, Or Neither?". The American Journal of Medicine. **132** (11): 1260–1261.
37. Goli G, Mukka R, Sairi S, (2016). Study of serum electrolytes in acute exacerbation of chronic obstructive pulmonary disease patients. International Journal of Research in Medical Sciences; 4:3324–3327.
38. Gould H.J, Sutton B.J, Beavil A.J, Beavil R.L, McCloskey N, Coker H.A, (2013). "The biology of IGE and the basis of allergic disease". Annual Review of Immunology. **21**: 579–628
39. Guilliams M., Bruhns P., Saeys Y., Hammad H., Lambrecht B.N.(2014). The function of Fcγ receptors in dendritic cells and macrophages. National Review in Immunology; 14:94–108.
40. Gupta G, Womer KL (2010). Profile of belatacept and its potential role in prevention of graft rejection following renal transplantation. Drug Description Development Therapy 4:375–82.
41. Gupta R.K, Lucas S.B, Fielding K.L, Lawn S.D, (2015). Prevalence of tuberculosis in post-mortem studies of HIV-infected adults and children in resource- limited settings: a systematic review and meta-analysis. AIDS. 29:1987–2002.
42. Gupta R.K., Lawn S.D., Bekker L.-G., Caldwell J., Kaplan R., Wood R (2013). Impact of human immunodeficiency virus and CD4 count on tuberculosis diagnosis: analysis of city-wide data from Cape Town, South Africa. International Journal of Tuberculosis and Lung Disease; 17:1014–1022
43. Jayasekera, J. P.; Moseman, E. A.; Carroll, M. C. (2007). "Natural antibody and complement mediate neutralization of influenza virus in the absence of prior immunity". Journal of Virology. **81** (7): 3487–94.
44. Hawn T.R., Day T.A., Scriba T.J., Hatherill M., Hanekom W.A., Evans T.G., Churchyard G.J., Kublin J.G., Bekker L., Self S.G (2014). Tuberculosis vaccines and prevention of infection. Microbiology Molecular Biology Review; 78:650–671.
45. Hendy R.M and El-Nagger M.E, (2019). Assessment of serum electrolytes (sodium, potassium, and ionized calcium) during chronic obstructive pulmonary disease exacerbation. The Egyptian Journal of Chest Diseases and Tuberculosis; 68:471–474.
46. Jiang Y., Liu H., Wan K (2014). MPT64 polymorphisms of Mycobacterium tuberculosis strains suggest ongoing immune evasion. Tuberc Edinb. ; 94:712–714.
47. Jindal SK, ed. (2011). Textbook of Pulmonary and Critical Care Medicine. New Delhi: Jaypee Brothers Medical Publishers. p. 549. ISBN 978-93-5025-073- 0.
48. Joosten S.A., Fletcher H.A., Ottenhoff T.H.M (2013). A helicopter perspective on TB biomarkers: pathway and process based analysis of gene expression data provides new insight into TB pathogenesis. Plos One; 8: 53-60.
49. Karumbi J, Garner P (2015). "Directly observed therapy for treating tuberculosis". The Cochrane Database of Systematic Reviews (5): CD003343.
50. Kaufmann S.H, (2010). Future vaccination strategies against tuberculosis: thinking outside the box. Immunity. **33** (4): 567–77.
51. Kaufmann S.H, (2011). Fact and fiction in tuberculosis vaccine research: 10 years later. Lancet Infectious Disease; 11:633–640.
52. Kaur J, Gitanjali G, Renu C, Mithilesh K.S, (2021). Evaluation of serum electrolyte status among newly diagnosed cases of pulmonary tuberculosis: an observational study. International Journal of Health and Clinical Research;4(5):219-222.
53. Kawakami C., Inoue A., Takitani K., Kanegane H., Miyawaki T., Tamai H (2011). X-linked agammaglobulinemia complicated with endobronchial tuberculosis. International Journal of Paediatrics; 100:466–468
54. Keitel W.A., Dai Z., Awe R.W., Atmar R.L., Morris S., Schneerson R., Robbins J.B (2013). Effects of infection and disease with Mycobacterium tuberculosis on serum antibody to glucan and arabinomannan: two surface polysaccharides of this pathogen. Biomedical Journal of Infectious Disease; 13:276.

55. Kim D.H, Cheon J.H, (2017). Pathogenesis of inflammatory bowel disease and recent advances in biologic therapies. Immune Network; 17:25–40.
56. Konstantinos A, (2010). "Testing for tuberculosis". Australian Prescriber; **33** (1): 12–18.
57. Kunnath-Velayudhan S, Salamon H, Wang H.Y, Davidow A.L, Molina D.M, Huynh V.T, Cirillo D.M, Michel G, Talbot E.A, Perkins M.D, (2010). Dynamic antibody responses to the Mycobacterium tuberculosis proteome. Proc. Natl. Acad. Sci. USA; 107:14703–14708.
58. Lawn S.D, Zumla A.I, (2011). "Tuberculosis". Lancet. **378** (9785): 57–72.
59. Lee J.J, Chan A, Tang T (2016). Tuberculosis reactivation in a patient receiving anti-programmed death-1 (PD-1) inhibitor for relapsed Hodgkin's lymphoma. Acta Oncol. 55:519–20
60. Liu L., Zhang W., Zheng J., Fu H., Chen Q., Zhang Z., Chen X., Zhou B., F eng L., Liu H., Jin Q (2014). Exploration of novel cellular and serological antigen biomarkers in the ORFeome of Mycobacterium tuberculosis. Molecular Cell Proteomics; 13:897–906.
61. Liu Q, Abba K, Alejandria M.M, Sinclair D, Balanag V.M, Lansang M.A, (2014). Reminder systems to improve patient adherence to tuberculosis clinic appointments for diagnosis and treatment. The Cochrane Database of Systematic Reviews (11): CD006594.
62. Lozano R, Naghavi M, Foreman K, Lim S, Shibuya K, Aboyans V, et al. Global and regional mortality from 235 causes of death for 20 age groups in 1990 and 2010: a systematic analysis for the Global Burden of Disease Study 2010.
63. Machado L.R., Bowdrey J., Ngaimisi E., Habtewold A., Minzi O., Makonnen E., Yimer G., Amogne W., Mugusi S., Janabi M., Aderaye G., Mugusi F., Viskaduraki M., Aklillu E., Hollox E.J (2013). Copy number variation of Fc gamma receptor genes in HIV-infected and HIV-tuberculosis co-infected individuals in sub-saharan Africa. PLoS One.
64. Mallery D.L, McEwan W.A, Bidgood S.R, Towers G.J, Johnson C.M, James L.C (2010). "Antibodies mediate intracellular immunity through tripartite motif- containing 21 (TRIM21)". Proceedings of the National Academy of Sciences, USA. **107** (46): 38-47.
65. McEwan W., Tam J.C.H., Watkinson R.E., Bidgood S.R., Mallery D.L., James L.C (2013). Intracellular antibody-bound pathogens stimulate immune signaling via the Fc receptor TRIM21. National Immunology; 3:12-18.
66. McShane H (2011). "Tuberculosis vaccines: beyond bacille Calmette-Guerin". Philosophical Transactions of the Royal Society of London. Biological Sciences. **366** (1579): 2782–89.
67. Moller M, Hoal E.G, (2010). "Current findings, challenges and novel approaches in human genetic susceptibility to tuberculosis". Tuberculosis. **90** (2): 71–83.
68. Monica, T. J.; Williams, S. B.; Goochee, C. F.; Maiorella, B. L. (2015). "Characterization of the glycosylation of a human IgM produced by a human-mouse hybridoma". Glycobiology. **5** (2): 175–185
69. Mummert H, Gradmann D (2001). "Action potentials in Acetabularia: measurement and simulation of voltage-gated fluxes". Journal of Membrane Biology. **124** (3): 265–273.
70. Naqash M.M, Bhat A.N, (2016). Immunoglobulin profile in pulmonary tuberculosis in endemically prevalent Kashmiri population, Kashmir, India. International Journal of Research in Medical Sciences; 4:5047-5051.
71. Niki M., Suzukawa M., Akashi S., Nagai H., Ohta K., Inoue M., Niki M., Kaneko Y., Morimoto K., Kurashima A., Kitada S., Matsumoto S., Suzuki K., Hoshino Y (2015). Evaluation of humoral immunity to Mycobacterium tuberculosis-specific antigens for correlation with clinical status and effective vaccine development. Journal of Immunologic Research; 527395.
72. Olalekan A.W, Oluwaseun F.A, Oladele H.A, Akeem A.D, (2015). Evaluation of electrolyte imbalance among tuberculosis patients receiving treatments in Southwestern Nigeria. Alexandria Journal of Medicine; 51, 255–260.
73. Palm N.W, Rosenstein R.K, Medzhitov R (2012). "Allergic host defences". Nature. **484** (7395): 465–72
74. Panteix G, Gutierrez MC, Boschiroli ML, Rouviere M, Plaidy A, Pressac D, . (2010). Pulmonary tuberculosis due to Mycobacterium microti: a study of six recent cases in France. Journal of Medical Microbiology. **59** (Pt 8): 984–989.
75. Parlowsky T, Welzel J, Amagai M, Zillikens D, and Wygold T, (2013). Neonatal pemphigus vulgaris: IgG4 autoantibodies to desmoglein 3 induce skin blisters in newborns. Journal of the American Academy of Dermatology; 48:623–625.
76. Patiroglu T., Akar H.H., van der Burg M., Unal E (2015). Autosomal recessive hyper IgM syndrome associated with activation-induced cytidine deaminase gene in three Turkish siblings presented with tuberculosis lymphadenitis - case report. Acta Microbiol Immunol Hung ;62:267–274.
77. Perley C.C., Frahm M., Click E.M., Dobos K.M., Ferrari G., Stout J.E., Frothingham R (2014). The human antibody response to the surface of Mycobacterium tuberculosis. PLoS One. 9:e98938.
78. Phuah J.Y., Mattila J.T., Lin P.L., Flynn J.L, (2012). Activated B cells in the granulomas of nonhuman primates infected with Mycobacterium tuberculosis. American Journal of Pathology;181:508–514.
79. Queval CJ, Brosch R, Simeone R, (2017). Mycobacterium tuberculosis. Frontiers in Microbiology. **8**: 2284.
80. Riesbeck K, and Nordstrom T, (2016). Structure and immunological action of the human pathogen Moraxella catarrhalis IgD-binding protein. Critical Reviews in Immunology; 26:353–376.

81. Rohini S.P, and Mahesh K.A, (2012). A Study on the Serum Immunoglobulin Levels in Pulmonary Tuberculosis Patients. International Journal of Bioscience, Biochemistry and Bioinformatics, Vol. 2, No. 4,279-281.
82. Romanowski K, Clark EG, Levin A, Cook VJ, Johnston JC (2016). Tuberculosis and chronic kidney disease: an emerging global syndemic. Kidney International; 90:34–40.
83. Roy A, Eisenhut M, Harris RJ, Rodrigues L.C, Sridhar S, Habermann S, (2014). "Effect of BCG vaccination against Mycobacterium tuberculosis infection in children: systematic review and meta-analysis". Biomedical Journal; **349**: g4643.
84. Sosa L.E, Njie G.J, Lobato M.N, Bamrah Morris S, Buchta W, Casey M.L, (2019). Tuberculosis Screening, Testing, and Treatment of U.S. Health Care Personnel: Recommendations from the National Tuberculosis Controllers Association and CDC, 2019. MMWR. Morbidity and Mortality Weekly Report. **68** (19): 439–443.
85. Stubbe H, Berdoz J, Kraehenbuhl J.P, Corthesy B, (2020). Polymeric IgA is superior to monomeric IgA and IgG carrying the same variable domain in preventing Clostridium difficile toxin A damaging of T84 monolayers. Journal of Immunology; 164:1952–1960.
86. Torrado E., Fountain J.J., Robinson R.T., Martino C.A., Pearl J.E., Rangel-Moreno J., Tighe M., Dunn R., Cooper A.M, (2013). Differential and site specific impact of B cells in the protective immune response to Mycobacterium tuberculosis in the Mouse. PLoS One.
87. Tosti, E (2010). "Dynamic roles of ion currents in early development". Molecular Reproduction and Development. **77** (10): 856–867
88. Williams A.F, and Barclay A.N, (2018). The immunoglobulin superfamily--domains for cell surface recognition. Annual Review of Immunology; 6:381–405.
89. Woof J.M, and Mestecky J, (2015). Mucosal immunoglobulins. Immunol Review; 206:64–82.
90. World Health Organization (WHO) (2010)."Tuberculosis Fact sheet N°104". . November. Archived from the original on 4 October 2006. Retrieved 26 July 2011.
91. Zimmermann N, Thormann V, Hu B, Kohler AB, Imai-Matsushima A, Locht C, (2016). Human isotype-dependent inhibitory antibody responses against Mycobacterium tuberculosis. EMBO Mol Med. 8:1325–39.
92. Zumla A, Hafner R, Lienhardt C, Hoelscher M, Nunn A (2012). Advancing the development of tuberculosis therapy. Nature Reviews. Drug Discovery. **11** (3):171–2.