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Original Research Article

Studies on Cell Adhesion and Thyroid Hormones in Patients with Pulmonary Tuberculosis Attending Clinic in IMSUTH, Orlu

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Abstract

This work was carried out to study Cell adhesion and thyroid hormones in patients with pulmonary tuberculosis attending clinic IMSUTH, Orlu. The study involves 60 Tuberculosis patients, comprising 20 active tuberculosis patients not on therapy, 20 tuberculosis on therapy for about three month and below ,20 tuberculosis patients on therapy for about 6 months and above, and 60 apparently healthy controls between the age of 20 and 55 years. The informed consent of all the subjects were sought and obtained. Some cell adhesion molecules determined were E-selectin, P-selectin and thyroid hormones T3 and T4 using Enzymes link lmmuno absorbent assay (ELISA).In carryout the work, about 5mls of venous blood were collected, allowed to clot and serum was obtained using pasture pipette. Data obtained were analyzed statistically using SPSS version 2.0 and results expressed as mean and standard deviation and the level of significance set at P <0.05. There were statistically significant increased levels(P<0.05) of P- selectin (16.86±0.84nm/ml) and E- selectin (30.36±3.42nm/ml) in active tuberculosis patients and those on therapy (12.84±1.22nm/ml) ,(19.85±1.90nm/ml) respectively when compared with controls(7.19±0.76nm/ml),(12.48±0.94nm/ml) respectively . Similarly, the levels of thyroid hormones, T3 (1.24±0.46ng/ml)and T4(7.99±1.60ug/dl)were not statistically significant (P<0.05) among active tuberculosis patients and those on therapy(1.21±0.66ng/ml)(7.60 ±1.40ug/dl) and even the controls (1.20±0.40ng/ml)(7.43±1.00ug/ml).The body mass index of the tuberculosis patients were significantly reduced when compared with body mass index of the apparently healthy controls (7,99±0.97kg/m2)(19.72±0.88kg/m2) respectively. This study shows that there is an increased level of E selectin and P selectin in pulmonary tuberculosis which suggests that selectin P and E may be involved in the pathogenesis of tuberculosis and also appear to be the most sensitive clinical measures of disease severity.

Keywords: Cell Adhesion, Thyroid Hormones, Pulmonary Tuberculosis

INTRODUCTION

Tuberculosis is an airborne disease caused by the bacterium *Mycobacterium tuberculosis*.[71] *Mycobacterium tuberculosis* is carried in airborne particles known as droplet nuclei , of 1-5 microns in diameter. These infection droplet nuclei are produced when person who have pulmonary or laryngeal Tuberculosis disease cough, sneeze, shout or sing.[26] Depending on the environment, these tiny particles can remain suspended in the air for hours.

Pulmonary tuberculosis (TB) is a contagious bacterial infection that involves the lungs. It is the most important tuberculosis infection , because an infection of the lungs is highly contagious due to the mode of droplet transmission. It may spread to other organ. *Mycobacterium tuberculosis* is transmitted through the air, not by surface contact. Transmission occur when a person inhales droplet nuclei containing *M . tuberculosis* ,
and the droplet nuclei traverse the mouth or nasal passages, upper respiratory tract , and bronchi to reach the alveoli of the lungs, the resulting lung infection is called primary tuberculosis.[16]

Most people recover from primary TB infection without further evidence of the disease. The infection may stay inactive (dormant) for years .In some people, it becomes active again .Most people who develop symptoms of a TB infection first becomes infected in the past. In some cases, the disease becomes active within weeks after the primary infection. Older adults, infants, people with weakened immune system for example due to HIV/AIDS are at higher risk of active TB or reactivation of TB[16].The rate of TB infection in a population can be increased due to some factors like , increase in HIV infections, increase in number of homeless people (poor environment and nutrition), presence of drug - resistant strains of TB.[16]

Tuberculosis remains a worldwide cause of increasing morbidity and mortality despite major advances in anti-TB drug administration and treatment (Godebo *et al*., 2015). According to WHO report 2017, 6.3 million new tuberculosis cases were reported in 2016.[74]

However , TB motility rate fell by 37 % in between 2000 to 2016.In spite of that ,the report has shown an increasing prevalence of the disease worldwide.[74]

Cell adhesion is the process by which cells interact and attach to neighbouring cells through specialised molecules of the cell surface . This process can occur either through direct contact between cell surface or indirect interaction, where cells attach to surrounding extracellular matrix , a gel – like structure containing molecules released by cells into spaces between them .[5]

Adhesion molecules are cell surface molecules , which bind to receptors or with soluble macromolecules present in extracellular membrane of host to promote cell adhesion and are involved in host pathogenesis.[73]Cell adhesion molecules (CAMs) are a subset of cell adhesion, proteins located on the surface involved in binding with other cells or with the extracellular matrix (ECM) in the process called cell adhesion .In essence, cell adhesion molecules help cells stick to each other and to their surroundings. It is an important component in maintaining tissue structure and function .These molecules play an important role in creating force and movement and consequently ensure that organs are able to execute their functions.[2]

There are four major super families or groups of cell adhesion molecules; the immunoglobulin superfamily of cell adhesion molecules (IgCAMs), Cadherins, integrins and the superfamily of c-type of lectin- like domains proteins (CTLDs). Proteoglycans are also considered to be a class of CAMs. One classification system involve the distinction between calcium –independent CAMs and calcium-dependent CAMs.[12]

Cells adhesion occurs from the interactions between cell adhesions molecules (CAMs), trans membrane proteins located on the cell surface .Cell adhesion links cells in different ways and can be involved in signal transduction for cells to detect and respond to changes in the surroundings. Alterationsin cell adhesion can disrupt important cellular processes and lead to a variety of diseases and also essential for infectious organisms, such as bacteria or viruses, to cause diseases.[5]

Several adhesion molecules found in mycobacteria such as fibronectin- binding proteins (FnBPs) and heparin-binding haemagglutinin (HBHA),which are involved in adherence and promote inter-malization of the *Mycobacterium tuberculosis* into the host cells, facilitate bacterial colonization .Interaction of these adhesions with host cell surface receptors not only helps in attachment and invasion but further exhibiting a cascade of signalling such as interferon (IFN)-Y response and activation of mitogen -activated protein kinase (MAPKs) pathway, which promotes pro- and or anti-inflammatory event by stimulating an immune response. Furthermore, adhesion molecule not only trigger the immune response but also interfere with the host signalling and modulate its intracellular mechanism . Hence exploiting the role of adhesion molecules is important to understand host pathogenesis inducted by *M.tuberculosis*.[73]

The clinical manifestation of tuberculosis is dependent on the cellular immune responses to the tubercle bacilli, characterized by the accumulation of monocytes/macrophages, Lymphocytes and polymorphnuclear leucocytes in tuberculosis lesions. Tuberculosis is characterised by the presence of activated mononuclear cells both in the peripheral circulation and in pleural fluid .Expression and up-regulation of adhesion molecules is the basis of cell- cell adhesion in granuloma formation and in leukocyte migration to the inflammatory site.It is well established that adhesion molecules play a fundamental role in the pathogen-host interaction. Invasion of host cells by bacteria is a complex process involving both bacterial and host cell determinant.[71]

Thyroid gland is an endocrine gland in the neck .It lies in the front of the neck in a position just below the Adams apples. The thyroid gland is made up of two lobes, the right lobe and the left lobe and these two lobes are joined by a small bridge of thyroid tissue called the Isthmus. The two lobes lies on either side of the wind pipe.[44]

The thyroid gland makes two hormones that are secreted into the blood. These hormones are key regulators of metabolism and development and are known to have pleiotropic effects in many different organs. The thyroid gland synthesizes and releases triodothyronine (T3) and thyroxine (T4), which represent the only iodine-containing hormones in vertebrates.T4 is the main product of thyroid secretion and local denomination in peripheral tissues produces T3, the biologically active thyroid hormone.T3 and T4 are bound to thyroglobulin, providing a matrix for their synthesis and a vehicle for their subsequent storage in the thyroid.

Thyroid gland is rarely affected by tuberculosis. It was once considered immune from the disease till Lebert in 1862 reported the involvement of the gland in a patient with disseminated tuberculosis. Tuberculosis of the thyroid is rare even in countries with high prevalence of tuberculosis[61].Tuberculosis of thyroid gland is extremely uncommon. The frequency of thyroid tuberculosis is 0.1 – 0.4% [70]. In the thyroid gland, the Tuberculous involvement may be in two main forms .Firstly ,military spread to the thyroid gland as part of generalized dissemination which is more common .The second one which is less-common is focal caseous tuberculosis of thyroid ,presenting as a localized swelling mimicking carcinoma.[70]

Tuberculosis is one of the oldest human pathogens emerging as the most important infectious disease of our times, and is the worldwide leading cost of increasing rate of morbidity and mortality despite major improvement in the anti-tuberculosis drug ministration and treatment .[50]

A previous study from Caucasians population indicates the cell adhesion molecules as a sensitive clinical measure of disease severity.[41]

There is inadequate information on the serum levels of thyroid gland in Tuberculosis globally and particularly in Orlu, Nigeria. Therefore this study is design to address this gap in knowledge.

MATERIALS AND METHODS

Study Area

This study was carried out in Imo state University Teaching Hospital,Orlu. This tertiary hospital serves as referral hospital for treatment of serious cases from Imo state and other neighbouring state and villages in South-East. Orlu,is the second largest city after Owerri,followed by Okigwe in lmo state with an estimated population of 420,000 as at 2006 census, located at 5º47 N 7ºO2¹20¹ E.

Study Population

A total number of 60 Tuberculosis patients (20 active Tuberculosis patients,20 on therapy for 3 months and below, and 20 on therapy for 6months and above) between the ages of 20-55 years were selected . They were age and sex-matched with 60 apparently healthy individuals (30 male and 30 female) who served as the control subjects. The exclusion criteria include individual less than 20 years ,history of any chronic disease like HIV/AIDs .

The selectin was done with the support of the physicians and the scientist in the TB outpatient department (TB DOT) of IMSUTH Orlu.The procedur eemployed also includes checking their weight and height.

Sample Collection

About 5 millilitres of venous blood was collected from each subject after checking their weight and height. The blood sample was dispensed into dry bottle, allowed to clot and then centrifuged to get the serum for the analysis. All blood samples was analysed within 4 days of collection.

Laboratory Assay

Selectin E was determined by using enzyme linked immune absorbent assay (Elisa) kit commercially provided by Melsin China

Triiodothyronine (T3) was determined using Accu-Bind Enzyme immunoassay test

Thyroxine (T4) was determined using Accu-Bind Enzyme immunoassay test system kit code no 3452-300(Accu Bind USA) described by Dunlap, 1990.

RESULTS

The results are presented as follows;

Table-4.1: Age and gender distribution of subjects

Age group(years)	Male	Female	Total
20-30	4	5	9
31-40	8	20	28
41-50	10	3	13
51-60	7	3	10
TOTAL	30	30	60

Out of the 60 tuberculosis samples obtained, the total number of patients with tuberculosis between the ages of (20 – 30) is 9 patients, (31 – 40) years of age is 28 patients, (41 – 50) years of ages is 13 patients and 51 and above is 10 pateitns. This age distribution shows that tuberculosis affects mostly people within the ages of 31.40 years.

Table-4.2: Mean ± S.D values of cell adhesion molecules (E selectin, P selectin) in TB patients with control subjects.

Parameters Mean ± SD	**TB Patients (n = 60)**	**Controls (n= 60)**	**P - value**
E - selectin(nm/ml)	23.36±5.58	12.48±0.12	0.00
P - selectin (nm/ml)	14.18±2.21	7.19±0.76	0.00

KEY: Statistically significant at P < 0.05

There was a significant increase (P< 0.05) in E – selectin of tuberculosis subjects when compared with the control 23.36 ± 5.58nm/ml and 12.48 ± 0.12nm/ml respectively**.** In P selectin there was also a significant increase of tuberculosis subjects when compared with the control 14.18 ± 2.21nm/ml and 7.19 ± 0.76nm/ml respectively (P<0.05)

Table-4.3: Mean ± S.D values thyroid hormones (T3, and T4)in TB patient with control subjects

Parameters Mean ± SD	**female TB patients (n = 30)**	**Female control (n=30)**	**P - value**
T3 (ng/ml)	1.22 ± 0.59	1.20 ± 0.40	0.803
T4(ug/dl)	7.73 ± 1.46	7.43 ± 1.00	0.185

KEY: Statistically significant at P <0.05

The mean ± S. D of T_3 shows that there was no significant difference (P> 0.05) 1.22 ± 0.56ng/ml and 1.20 ± 0.40ng/ml respectively of the tuberculosis subjects and the control. The mean ± S.D of T4 also shows that there was no significant difference (P>0.05) between the tuberculosis subjects and the controls 7.73 ± 1.46 ug/dl and 7 .43 ± 1.00 ug/dl respectively.

Table-4.4: Comparative analysis of cell adhesion molecules (Serum E – selectin, P selectin), in newly diagnosed TB Patients and control subjects.

Variables Mean ± SD	**Newly Diagnosed (n = 20)**	**Control (n=20)**	**P - value**
E - selectin (nm/ml)	30.36±3.42	12.25±0.84	0.00
P - selectin (nm/ml)	16.87±0.84	7.20±0.75	0.00

KEY: Statistically significant at P < 0.05

There was a significant increase (P<0.05) in E selectin of newly diagnosed TB subjects when compared with the control 30.36 ± 3.42nm/ml and 12.25 ± 0.84nm/ml respectively. In P selectin, there was also a significant increase in newly diagnosed TB subjects when compared with the controls 16.87 ± 0.84nm/ml and 7.20 ± 0.75nm/ml respectively.

Table-4.5: Comparative analysis of thyroid hormones (T3, T4) in newly diagnosed TB patients and control subjects.

Parameters Mean ± SD	**Newly diagnosed (n=20**	**Control (n=20)**	**P - value**
T3 (ng/ml)	1.24±0.46	1.22±0.45	0.853
T4(ug/dl)	7.99±1.60	7.02±0.65	0.018

KEY: Statistically significant at P < 0.05

T3 - Triiodothronine
T4 –Thyroxine

There was no significant difference in the levels of T_3 of newly diagnosed and that of the control (PP>0.05), 1.24 ± 0.46ng/ml and 1.22 ± 0.45ng/ml respectively. The mean ± S.D of T_4 in newly diagnosed subjects were not significant (P>0.05) 7.99 ± 1.60ug/dl and 7.02 +_0.65ug/dl respectively when compared with the controls.

Table-4.6: Comparative analysis of cell adhesion molecules (E selectin and P Selectin) among TB patients on therapy with control subjects.

Parameters Mean ± SD	TB on therapy (n=20)	Control (n=20)	P - value
E – Selectin(nm/ml)	19.85 ± 1.90	12.48 ± 0.94	0.00
P Selectin (nm/ml)	12.84 ± 1.22	7.19 ± 0.76	0.00

The Mean ± S.D levels of E – selectin of TB patients on therapy was significantly increased (P<0.05) when compared with the control, 19.85 ± 1.90nm/ml and 12.48 ± 0.94nm/ml respectively. There was also a significant increase (P<0.05) in P selectin of TB patients on therapy when compared with the control 12.84 ± 1.22 nm/ml and 7.19 ± 0.76nm/ml respectively.

Table-4.7: Comparative analysis of thyroid hormones (T3 and T4) among TB patients on therapy with control subjects.

Parameters Mean ± SD	TB on therapy (n=20)	Control (n=20)	P - value
T3(ng/ml)	1.21 ± 0.66	1.20 ± 0.40	0.910
T4 (ug/dl)	7.60 ± 1.40	7.43 ± 1.00	0.488

KEY: Statistically Significant at P <0.05

T3 – Triiodothronine
T4 - Thyroxine

The mean ± S.D levels of T3 shows that there was no significant difference (P>0.05) in TB patients on therapy and controls subjectives, 1.21 ± 0.66ng/ml and 1.20 ± 0.40ng/ml respectively. There was also no significant different (P>0.05) in T4 levels of TB patients on therapy and control subject, 7.60 ± 1.40ug/dl and 7.43+_1,00.ug/dl.

Table-4.8: Comparative analysis of cell adhesion molecules (E selectin and P selectin) among newly diagnosed, 3 months and 6 months on therapy

Parameters Mean ± SD	Newly diagnosed TB patients (n = 20)	TB patients on therapy(< 3months) (no=20)	TB patients on therapy (> 6months) (no=20)	Control (n=20)	P - value
E - selectin (nm/ml)	30.36±3.42	21.26±0.70	18.45±1.66	12.25 ± 0.84	0.00
P - selectin (nm/ml)	16.86±0.84	13.03±1.56	12.66±0.72	7.20 ± 0.75	0.00
T3 (ng/ml)	1.24±0.46	1 .40±0.84	1.03±0.35	1.22 ± 0.45	0.1394
T4(ug/dl)	7.99±1.66	7.77±1.41	7.44±1.38	7,02 ± 0.65	0.505

KEY: Statistically significant at P <0.05

T3 –Triiodothyronine
T4 - Thyroxine

There was a significant increase (P< 0.05) in E selectin of newly diagnosed TB patients when compared with those on therapy for 3 months and below, 6 month and above and control. 30.36 ± 3.42nm/ml, 21.26 ± 0.70nm/ml, 18.45 ± 1.6nm/ml,6, 12. 25nm/ml ± 0.84nm/ml respectively. In P selectin there was also a significant increase of TB patient of newly diagnosed, when compared with those on therapy for 3 months and below 6 months and above.

The mean ± S.D of T3 shows that there was no significant difference (P>0.05) 1.24 ± 0.46nm/ml, 1.40 ± 0.84nm/ml, 1.03 ± 0.35nm/ml respectively.

The mean ± S.D of T4 also shows that there was no significant difference (P>0.05).

Table4.8.1: Comparative analysis of cell adhesion molecules(E seletin,P selectin) and thyroid hormones (T3,T4)among male TB Patients with Male Control Subjects.

Parameters	Male TB Patient (n=30)	Male Control (n=30)	P Value
E selectin(nm/ml)	23.48±5.78	12.59±0.95	0.00
P selectin(nm/ml)	14.09±2.09	7.26±0.76	0.00
T3 (ng/ml)	1.22±0.75	1.17±0.30	0.77
T4 (ug/dl)	7.57±1.44	7.61±1.06	0.88

KEY: Statistically significant at P< 0.05

T3 – Triiodothyronine
T4- Thyroxine

The mean ± S.D levels of E selectin were significantly elevated in male TB patients when compared with male control subjects, 23.48 ± 5.78nm/ml, 12.59±0.95nm/ml respectively. P selectin were significantly increased in male TB patients when compared with male control subjects,14.09±2.09nm/ml, 7.26±0.76nm/ml respectively. Also there was no significant difference between T3and T4 of Male TB Patients with the control subjects (P =0.77) (P = 0.88)respectively.

Table-4.8.2: Comparative analysis of cell adhesion molecules (E selectin and P selectin) and thyroid hormones (T3 and T4) among female TB patients with females control subjects.

Parameters Mean ± SD	TB Patients (female) (n=30)	Control (n=30)	P - Value
E Selectin(nm/ml)	23.74 ± 5.25	12.38 ± 0.90	0.00
P Selectin(nm/ml)	14.43 ± 2.33	7.12 ± 0.77	0.00
T3(ng/ml)	1.26 ± 0.41	1.24 ± 0.41	0.845
T4(ug/dl)	7.83 ± 1.51	7.21 ± 0.92	0.068

KEY: Statistically Significant at P < 0.05

T3: Triiodothyronine
T4: Thyroxine

The mean ± S.D levels of E selectin were significantly increased in female TB patients when compared with control subjects 23..74±5.25nm/ml,12.38±0.90nm/ml respectively.The mean ± S.D. of P selectin were significantly increased in female TB patients when compared with control subjects 14.43 ± 2.33ng/ml, 7.12 ± 0.77nm/ml respectively. Also there was no significant different between T3, T4 and control subjects of TB when compared with control (P = 0.845,P = 0.068) respectively

Table-4.9: To evaluate anthropometric indices of tuberculosis patients with the control subjects

Parameters Mean ± SD	TB Patients (female) (n=60)	Control (n=60)	P - Value
BMI(kg/m2)	7.99± 0.97	19.72 ± 0.88	0.00

The mean ± S.D levels of body mass index of TB patients was significantly reduced (P<0.05) when compared with control subject (7.99 ± 0.97kg/m ^{2}, 19.72 ± 0.88kg/m respectively.

DISCUSSION

Pulmonary Tuberculosis is an airborne disease caused by the bacterium *Mycobacterium tuberculosis* (M.Tuberculosis). A contagious bacterial infection that involves the lungs, and can spread from there to other organs. Pulmonary tuberculosis is curable with an early diagnosis and antibiotic treatment. Tuberculosis remains a major public health challenge in Orlu, Imo state Nigeria, because of the increasing morbidity and mortality rate. Effective tuberculosis management has been shown to reduce the incidence.[41]

Data from this study showed a higher level of selectin E and selectin P in all the tuberculosis patients compared with controls and there were no significant different in the level of thyroid hormones. Also the body mass index of Tuberculosis patients were significantly reduced compared with controls.

This increase or higher levels of E selectin and P selectin obtained from all tuberculosis patients may be as a result of distinct profile of soluble adhesion molecules facilitating host pathogens interacting and mediating *Mycobacterium Tuberculosis* pathogensis.[22]

It was observed from this study that the levels of E selectin and P selectin were significantly reduced on tuberculosis patients on therapy when compared to active tuberculosis patients, this may indicates the important if cell adhesion molecules in the pathogenesis of inflammatory lungs disease.

Similarly, it was observed from this study that the levels of selectin P and selectin E were significantly decreased in pulmonary tuberculosis patients on therapy for six (6) months when compared to the tuberculosis patients on therapy for three (3) months, may suggest that therapeutic treatment reduces the levels of P and E selectin in patients with pulmonary tuberculosis and hence the severity of diseases is also reduced. Furthermore, it was observed that the levels of selectin P and E decreases as the duration of medication increases. This is an indication that therapeutic treatment reduces the levels of selectin P and selectin E in patients with pulmonary tuberculosis[41].

Also in male Tuberculosis patients compared with male controls and in female tuberculosis pateitns compared with female controls. There were significant increase in the level of P and E selectin in male tuberculosis patients compared with male controls and female tuberculosis patients compared with female controls. Therefore the higher level of P and E selectin observed in both male and female tuberculosis patients may be indication that cell adhesion molecules are involved in the pathogensis of inflammatory lung disease and most sensitive marker for pulmonary tuberculosis disease severity.[41]

This study revealed that there was no significant difference in the levels of thyroid hormones in patients with active pulmonary tuberculosis when compared to tuberculosis patients on therapy and controls. This might indicate that thyroid hormone may be rarely affected in both active tuberculosis and treated diseases in this environment. This may be as a result of bactericidal attributes of the thyroid and high levels iodine in the gland. Previous studies have reported that thyroid hormone is rarely affected by tuberculosis.[4]

Also it was observed from this study that the body mass index of the tuberculosis patient are reduced when compared with control subjects which suggests that low BMI might be associated with increased risk of tuberculosis. This is in line with the work of Kim *et al*.,(2018).There is increasing evidence that under nutrition in active TB patient is associated with an increased frequency and severity of disease.

CONCLUSION

The results of this study have shown that P and S selectins status are significantly increased in active tuberculosis which supports the possibility that some cell adhesion molecules may be involved in the pathogenesis of tuberculosis. This could probably imply that there is distinct profile of adhesion molecules in active pulmonary tuberculosis and that E and P selectins appear to the most sensitive clinical measures of disease severity. Thyroid hormones is rarely affected in tuberculosis, which might be as a result of bactericidal attribute of the thyroid Tuberculosis remains an important public health challenge in Orlu, Imo State, because it associates with poverty, which in turn drives malnutrition, leading to cause of mortality worldwide, especially in low and medium income states where its incidence is the highest and drug resistant TB has developed into an escalating problem consequences.[66]

REFERENCES

1. Adkinson, N., Bennett, J., Douglas, R. and Mandell, G. (2010). Mandell, Douglas and Benneth's principles and practice of infectious diseases(7th edition). Philadelphia, PA: Churchill livingstone/Elsevier. P .250
2. Agwunobi, K., Okoroiwu, L., Nnodim, J. and Akujobi, A. (2020). Association of cell adhesion molecules, glycated haemoglobin and some haematalogical parameters with Diurnal Variation of blood pressure among Hypertensives. *Archives of Nephrology*. 2(2):01-07.
3. Ahmed, N. and Hasnain, S. (2011). Molecular epidemiology of tuberculosis in india: moving forward with a systems biology approach. *Tuberculosis*. 91(5): 407-413.
4. Ajay k., Mayank M., Ved F., Surya K., Singh H., Neha K., (2019).Tuberculosis of the thyroid gland. *Muller Journal of Medical Sciences and Research*.8; 52-54.
5. Albert B., Johnson A., Lewis J., Morgan D., Raff M., Roberts K., Walker P.,(2014). Molecular Biology of the cell. (6th edition). Garland science. 94(7): 575-581.
6. Amalia A K,and Mohd R A(2015).Review of cell adhesion studies for Biomedical and Biological Applications. *Internal Journal of Molecular Sciencees.16* (8); 18149-18184.
7. Barnes, T., Amir, E. and Hype (2017). The prognostic value of infiltrating immune cells in cancer. *British Journal for cancer*. 117: 451-458.
8. Behera, D. (2016). Textbook of pulmonary medicine (2nd edition). New Delhi: jaypee brother's medical publishers. P.457.
9. Bendas, Gerd; Borsig, Lubor (2012). Cancer Cell Adhesion and Metastasis: Selectins, Integrins, and the Inhibitory Potential of Heparins. *International Journal of Cell Biology.* 7:54-55.
10. Borisov, A., Bamrah, M., Njie, G., Winston, C., Burton, D. and Goldberg, S. (2018). Update of recommendations for use of once-weekly isoniazid-rifapentine regimen to treat latent; mycobacterium tuberculosis infection MMWR. *Morbidity and mortality weekly report*. 67(25): 723-726.
11. Boron, W. and Boulpalp, E. (2012). Medical physiology (2nd edition). Philadelphia; saunder.p. 1052-1053.
12. Brackenbury R., Rutishauser U., Edelman, S., (2017). Distinct calcium independent and calcium - dependent adhesion systems of chicken embryo cells. Proceedings of the National Academy of sciences of the United States of America. 78(1): 387-391.
13. Brown K.,and Yamada K.,(2015).ThebRole of lntegrins during Vertebrae Development. *Developmental Biology* .6(2):69-77.
14. Bulbuloghi, H., Ciralik, E., Okur, G., Ozdemiv, E. and Ezberci, A. (2006). Tuberculosis of the thyroid gland; review of the literature. *World journal of surgery.* 30(2):149-155.
15. Buxton,R.,and Magee,A.,(2012).Structure and interactions of desmosomal and other cadhrins.*Seminars in Cell and Developmental Biology*.3 (3):157-167.
16. Centres of disease control and prevention (CDC) (2011). Division of tuberculosis elimination. P.24 'core curriculum on TB, what the clinician should know.
17. Chi C., Leung.,Tai H.,Lam.,Wai M.,Chan(2017).Lower Risk of Tuberculosis in Obesity. *Journal Internal Medicine*.167;1297-1304.
18. Chothia, C. and Jones, E. (2017). The molecular structure of cell adhesion molecules. *Annual review of biochemistry*. 66: 823-862.
19. Cury. A., Meira, V., Monte, O.,Marone, M. and Scalissi (2012). Clinical experience with radioactive iodine in the treatment of childhood and adolescent Grave's disease. *Endocrine connection*. 2(1):32-37.
20. Chiang,A.C and Massague,J(2018).Molecular basis of metastesis.*The New England Journal of Medicine*.359(26)2752-2823.
21. Darga B.,and Laxman M.,(2019).Adhesion Molecules facilitate host pathogen interaction and mediate mycobacterium tuberculosis pathogenesis.*Journal of Medical Research*.150;1-23.
22. Fridman, W., Pages, F., Sautes-Fridman, C. Galon, J. (2012). The immune contexture in human tumours; impact on clinical outcome. *Nature Reviews Cancer.* 12:293-299.
23. Freidl,P.,and Wolf, K.,(2013).Turmour cell invasion and migration:diversity and escape mechanisms.*Nature Reviews Cancer*,3(5)362-368.
24. Garman, E. F. (2015). Antiviral adhesion molecular mechanisms for influenza: W. G. Laver's lifetime obsession. Philosophical Transactions of the Royal Society B: Biological Sciences. 370-372
25. Glaziou, P., Floyd, K. and Raviglione, M. (2018). Global epidemiology of tuberculosis. *Semin respiratory critical care medicine*. 39:271-285
26. Godedo, A., Woldi, A.and Toma, A. (2015). Recent advances in the development of anti-tuberculosis drugs acting on multidrug resistance strains, *Internal Journal Research Pharmacological Bioscience* 2:1-8.
27. Guyton and Hall (2011). Page 907, 939.
28. Hamzaoui A.,Hamzaoui K.,Kahan A.,Chabbou A.,(2016),Levels of soluble VCAM-1,soluble ICAM-1,and soluble E-selectin in patients with tuberculosis.Institute of Chest Diseases,5; 276-279.

29. Hanna, Suhair; Etzioni, Amos (2012). Leukocyte adhesion deficiencies. Annals of the New York Academy of Sciences. 1250 (1): 50–51
30. Harris, Estelle S., Weyrich, Andrew S., Zimmerman, Guy A. (2012). Lessons from rare maladies: leukocyte adhesion deficiency syndromes. Current Opinion in Hematology. 20 (1): 16–25.
31. Harris, Tony J. C.; Tepass, Ulrich (2010). Adherens junctions: from molecules to morphogenesis. Nature Reviews Molecular Cell Biology. 11 (7): 502–514.
32. Hawn, T., Day, T., Scriba, J., Hatherill, M., Hanckom, W. and Evans, G. (2014). Tuberculosis vaccines and prevention of infection. *Microbiology and Molecular Biology*. 78(4):650-671.
33. Humphries,J.,Byron, A.,and Humphries, M.,(2016).Integrin ligands at a glance. *Journal of Cell Science*.119 (19) 3901-3903.
34. Jia W.,Wang R.,Zhao J.,Lou I.,Zhang D.,Wang X.,and Han X.,(2011).E Selectin expression increases in human cerebral aneurysm tissues.*The Canadian Journal of Neurological Sciences*,38(6):858-862.
35. Jindal, S. (2011). Textbook of pulmonary and critical care medicine. New Delhi: jaypee brother's medical publishers. P.525-528.
36. Johnson, R.L., (2019). Cell adhesion molecules in the development and progression of malignant melanoma.*Cancer and Metastasis Reviews*,18(3)345-357.
37. Kielstra, P. and Tabary, Z. (2014). Ancient enemy, modern imperative- A time for greater action against tuberculosis. Economist intelligence unit.4 (4):284-294.
38. Kim S.,Ye S.,Ha E.,Chun E.,(2018).Association ofbody mass index with incident tuberculosis in Korea. *Journal .prone.*13:4-10.
39. Krachler, Anne Marie; Orth, Kim (2014). Targeting the bacteria–host interface. Virulence.*Journal of HIV/AIDS in infectious diseases* 4 (4): 284–294.
40. Lai C.,Wong K.,Chan K.,Ho S.,Chung S.,Haskard D.,(2013),Circulating Adhesion Molecules in tuberculosis.*Journalof Clinical Immunology*.94;3-5
41. Lawn, s. and Zumla, A. (2011) Tuberculosis. *Lancent.* 378(9785): 57-72.
42. Ley,K.(2013).The role of selectin in inflammation and disease.*Trends in Molecular Medicine*,9(6):263-276.
43. Lodish, Harvey.,Berk ,Arnold.,Zipursky, Lawrence., Matsudaira ., Paul, Baltimore,David., and Darnll James (2014).Cell-Cell Adhesion and Communication. *Journal of Cell Biology*. 159:332-341.
44. Magner James (2014). Historical note; many steps led to the discovery of thyroid stimulating hormone, European thyroid stimulating hormone. *European Thyroid Journal*. 3: 95-100.
45. Mateo M, Generous, A.Sinn, P. L., Cattaneo, R. (2015). Connections matter - how viruses use cellcell adhesion components, *Journal of Cell Science*. 128 (3): 431–439.
46. McEver, Rodger P. (2015). Selectins: initiators of leucocyte adhesion and signalling at the vascular wall. Cardiovascular Research. 107 (3): 331–339.
47. Melmed, S., Polonsky, k., Larsen, P. and Kronenbery, H (2011). Williams textbook of endocrinology (12th edition) saunders. P. 331-336.
48. Michelle, Maclsaac, Richard, Grossmann, Mathis (2017). Hypothyroidism-investigation and management. The royal Australian college of General Practitionery.6;9-13
49. Michelle B.,and Suman L.,(2019)Mycobacterium tuberculosis primary infection and Dissemination; A Critical Role for Alveolar Epithelial cells.Department of Patholog ,New York,United State.
50. Nguyen,T.H.,(2014)Mechanisms of Metastesis. *Clinics in Dermatology*.22 (3):209-218.
51. Nicholl ID, Matsui T, Weiss TM, Stanley CB, Heller WT, Martel A, Farago B, Callaway DJ, Bu Z (2018). Alpha-catenin structure and dynamics in solution and in complex with F-actin. *Biophysical Journal.* 115 (4): 642–654.
52. Nnodim J.,Diala T.,Ndunelo C.,Nwajiaku V., Nwanebu C., (2019) Role of cell adhesion molecules in Medical laboratory Diagnosis. Archives of Nephrology.2:16-28.
53. Okur, E. and Halezeroglu, S. (2014). Thoracic surgery for haemolysis in the context of tuberculosis; what is the best management approach. *Journal of Thoracic Disease*. 6(3): 182-185.
54. Picker T., and Louis I.,(2014).Control of Lymphocyte homing. *Current Opinion in Immunology*.6 (3)394-406.
55. Pilo, A., Lervasi, G., Vitek, F., Ferdeghini, M., Cazzuola, F., Bianchi, R. (2017). Thyroidal and peripheral production of 3,5,3- triiodothyronine in humans by multicompartmental analysis. *The American Journal of Physiology*. 258: 715-726.
56. Quyyumi A.,Dakak N.,Andrews N.,Husain S., Arora S.,Gilligan D.,and Panza J.(2015).Cannon ROIII:Nitric oxide activity in the human corcnary circulation.Impactof risk factors for coronary atherosclerosis. *Journal of Clinical Investigation*. 95:1747-1755.
57. Rawat, R., Monu, Meena, L. (2015). Adhesion molecules, a potent surface marker of mycobacterium play key role in host- pathogen interaction and pathogenesis. Advance research journal of chemical biotechnology 2:41-46.
58. Restrepo, B. (2007). Convergence of the tuberculosis and diabetes epidemics; renewal of old acquaintances. *Clinical Infectious Diseases.* 45(4):436-438.
59. Reinout Van Crevel.(2012),Decreased Plasma Leptin Concentration in Tuberculosis Patients are Associated with Wasting and Inflammation. *Journal Clinical Endocrinology Metabolism.*4:72-80.

60. Roberto A., Federico.,Diaz G., Francisco S.,(2012).Adhesion Molecules in lnflammatory Diseases. *England Journal Medical*.56; 977-988.
61. Sant, P., Parul, T., Sneh, S., Sanjay, K. (2012). Primary tuberculosis of the thyroid gland: a case report. *Asian Pacific Journal of Tropical Biomedicine* 2(10):839-840.
62. Schweizer, U. and Steegborn, C. (2015). Thyroid hormones from crystal packing to activity to reactivity. *Angewandte chemie* 54(44): 12856-12858.
63. Singh, Ram Sarup, Walia, Amandeep Kaur, Kanwar, Jagat Rakesh (2016). Protozoa lectins and their role in host–pathogen interactions. Biotechnology Advances. 34 (5): 1018–1029.
64. Soo Jung Kim, Shinhee Ye, Ye Ji Han,Eunhee Ha, Eun Mi Chun.(2017) .The Association of body mass index with incidence of tuberculosis in Korea.*European Respiratory Journal*.50:27-29.
65. Sterling, T., Njie, G., Zenner, D., Cohn, d., Reves, R. and Ahmed, A. (2020). Guildelines for the treatment of latent tuberculosis infection: recommendations from the national tuberculosis controllers association and CDC. MMWR. Recommendations and reports 69(1): 1-11.
66. Subotic D.,Yablonskiy P.,Sulis G.,(2016)Surgery and pleura-pulmonary tuberculosis ;a scientific literature review. *Journal of Thorac Disease*.8:474-485.
67. Sumigray, Kaelyn D.; Lechler, Terry (2015). Cell Adhesion in Epidermal Development and Barrier Formation. Current Topics in Developmental Biology. 112; 383–414.
68. Tamgadge, Sandhya; Bhatt, DaivatM; Pereira, Treville; Tamgadge, Avinash; Bhalerao, Sudhir (2011). Pemphigus vulgaris. Contemporary Clinical Dentistry. 2 (2): 134–137.
69. Tanaka, A. and Sakaguchi, S. (2017). Regulatory T-cells in cancer immunotherapy. *Cell Researches*. 27:109-118.
70. Uzoma M. and Najmul I., (2011). Thyroid tuberculosis access series and a *Review Journal of thyroid Research* 10:4061-4067.
71. Viveshree S., Govender T., Saiyur R., Manormoney P., (2014). Mycobacterium tuberculosis adhesion; potential biomarkers as anti-tuberculosis therapeutic and diagnostic targets. *Journal of medical microbiology and infection control*. 160:1821-1831.
72. Who (2011). The sixteen global report on tuberculosis.
73. Wolters Kluwer. (2019). Adhesion molecules facilitate host-pathogen interaction and mediate mycobacterium tuberculosis pathogenesis; *Indian Journal Medical Research*. 4: 3-5.
74. World Health Organization (2017). Global Tuberculosis Report.
75. World health organization (WHO)(2015). Tuberculosis fact sheet .104
76. World health organization (WHO)(2018). Tuberculosis (TB)