IMAGE: A MAP OF THE STARS OF THE ORION CONSTELLATION

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ABSTRACT

Vaginal Infection is the most common problem which almost most girls suffer. It is neglected but it has a serious effect if it is not treated. It is diagnosed if the color of the vaginal discharge changes, has a strong fishy odor, irritation, and burning sensation. The normal microflora of the vagina, act as the first line of defense in preventing the infection from pathogenic fungi, bacteria or protozoa which can cause vaginal infection. Several treatment strategies have been adapted for vaginal infections. Vaginitis trigger UTI (Urinary Tract Infection) in most of the girls. This review, is focused on vaginal infections caused by different types of microorganisms, symptoms and their treatment method.

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Strategies for Managing Vaginal Infection

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ABSTRACT

Vaginal Infection is the most common problem which almost most girls suffer. It is neglected but it has a serious effect if it is not treated. It is diagnosed if the color of the vaginal discharge changes, has a strong fishy odor, irritation, and burning sensation. The normal microflora of the vagina, act as the first line of defense in preventing the infection from pathogenic fungi, bacteria or protozoa which can cause vaginal infection. Several treatment strategies have been adapted for vaginal infections. Vaginitis trigger UTI (Urinary Tract Infection) in most of the girls. This review, is focused on vaginal infections caused by different types of microorganisms, symptoms and their treatment method.

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I. INTRODUCTION

A healthy vagina contains some bacteria and a few yeast cells to maintain the natural balance of the vagina, whenever the number of bacteria and yeast cells goes imbalanced it leads to several vaginal infections [1]. Irritation and swelling of the vagina and vulva with unusual vaginal discharge which has a strong odour, and pain with a burning sensation during urination, are common symptoms of vaginal infection [2].

Whenever these symptoms occur, it causes discomfort and distress which lead women to seek medical consultation [3]. In the entire world, 3 out of 4 women suffer from vaginal infections once in their lifetime. The most common vaginal infection seen in women is bacterial vaginosis caused by bacteria, Candidal vaginitis caused by the fungus, and trichomoniasis which is caused by protozoa [4, 5, 6].

II. BACTERIAL VAGINOSIS

Bacterial vaginosis is the most common infection during the reproductive age of women it causes abnormal discharge and inflammation of the vagina [7, 8]. It is the most common infection in women. Bacterial vaginosis is occurred due to the replacement of the regular Lactobacillus bacteria with Prevotella, Mobiluncus, Ureaplasma, *Gardnerella vaginitis*, Mycoplasma, and many other uncultivated anaerobes [9, 10, 11]. *Lactobacillus* which is present normally in the vagina produces bacteriocins, lactic acid, and hydrogen peroxide, which help to maintain an acidic pH, and protect against other infections in the vagina [12, 13]. An enzyme produced by the bacteria which causes bacterial vaginosis degrades the gel layer protection of the vaginal epithelium and cervical [14]. They produce inflammatory proteins which associate with complications that occur during pregnancy like preterm labor and birth [14, 15], endometritis, gynecologic surgery, *Neisseria gonorrhoeae, Chlamydia trachomatis,* pelvic inflammatory disease, increased susceptibility to HIV type 1, and herpes simplex virus type 2 [16, 17, 18].

1. SYMPTOMS

- Burning during urination
- Thin, gray, white, or green vaginal discharge
- Vaginal itching
- Foul-smelling 'fishy' vaginal odor [19, 20]

2. RISK FACTOR

Bacterial vaginosis is not a sexually transmitted infection (STI) [21], but it resembles trichomoniasis, Chlamydia, and gonorrhea which are sexually transmitted infections [22]. Douching, having male partners who have sex with other women, having a new partner, having sex with women, use of an intrauterine device, use of an inconsistent condom, cigarette smoking, and black ethnicity [23, 24]. The use of oral contraceptives has an inverse relation with acquiring bacterial vaginosis [25].

3. DIAGNOSE

Bacterial vaginosis can be diagnosed by the BV test other names are the KOH test, wet mount test, and vaginal pH test [26, 27]. BV tests are done similarly to a Pap smear or pelvic exam. For the BV test Gram stain is the criterion standard to diagnose [28]. The Nugent score which is a Gram stain scoring system for vaginal swabs to diagnose bacterial vaginosis [29], a score of 0 to 3 is considered normal vaginal flora, 3 to 7 are the intermediate which is not identified for any abnormal or normal, and 7 to 10 is over to bacterial vaginosis [30, 31]. Amsel criteria are another method to make a clinical diagnosis of bacterial vaginosis [32]. The following are considered diagnostic for bacterial vaginosis: the fishy odor of discharge, homogenous gray-white vaginal discharge, vaginal pH greater than 4.5, or clue cells on the saline wet mount [33, 34, 35].

Currently, three other tests are being practiced in clinical diagnosis: BVBLUE (Gryphus diagnostics, Knoxville, Tennessee) is a rapid point of care test when mixed with a vaginal swab it will turn blue if there is any elevation of sialidase activity is produced by the bacterial pathogens which are associated with bacterial vaginosis [36, 37].

Pip activity test card (San Diego, Quidel corporation, California) is also a rapid test for confirming bacterial vaginosis by identifying an enzyme produced by *Gardnerella vaginalis* [38].

Affirm VPIII (Becton Dickinson, Maryland, Sparks) is a DNA probe-based test that helps to measure the level of Gardnerella vaginalis [39]. All these tests perform similarly to the gram stain. One may feel mild discomfort when the speculum is put inside the vagina to take the sample [40].

There are chances of bacterial vaginosis infection to reoccur after successful treatment [41], if the diagnosed person is pregnant then it is important to treat the infection, it can cause health problems to the unborn baby [42, 43].

4. TREATMENT

For the treatment of bacterial vaginosis, the doctor may prescribe one of the following medications:

Clindamycin (Cleocin, Clindesse): it is available as a cream that is inserted into the vagina [44].

Secnidazole (Solosec): is an antibiotic taken orally in one dose. This medication comes as a packet of granules that is sprinkled onto a soft food, such as pudding or yogurt, and should eat the mixture within 30minutes, and be careful not to chew or crunch the granules [45, 46].

Metronidazole (Metrogel-vaginal, Flagyl): this medicine is taken orally as a pill, and is also available as a topical gel that can be inserted into the vagina. One can get the risk of abdominal pain, stomach upset, or nausea while using this medication. During treatment, one should avoid alcohol [47].

Tinidazole (Tindamax): even this medication is taken orally. Tinidazole also has the potential to cause stomach upset and nausea same as oral metronidazole, while treatment period one should avoid alcohol for at least three days after completing the treatment [48, 49].

III. CANDIDAL VAGINITIS

Candidal vaginitis is the second most common cause of vaginitis after bacterial vaginosis [50]. The vaginal yeast is caused by the *Candida albicans* strain, and the majority of non-albicans cases are caused by the *Candida glabrata* strain [51, 52]. These organisms may also be present in asymptomatic women [53], the non-albicans fungi are more resistant to the treatment than the Albicans species [54]. The non-albicans candidiasis strain causes severe candidal vaginitis infection, it becomes complicated in women with uncontrolled diabetes, immunosuppression or debilitation, or pregnant women. There are high chances of recurrent candidal vaginitis [55, 56].

The *Albicans candidiasis* strain causes mild to moderate candidal vaginitis, the etiology is likely to be *Candida albicans*, it is non-immuno-compromised in women and it is infrequent or sporadic [57].

1. SYMPTOMS

- Vaginal rash
- Watery vaginal discharge

- Vaginal pain and soreness
- thick, white, odor-free vaginal discharge with a cottage cheese appearance
- Irritation and itching in the vagina and vulva
- redness and swelling of the vulva
- a burning sensation, during urinating or while intercourse [58, 59]

2. RISK FACTOR

Recent antibiotic use is a significant risk factor for acquiring candidal vaginitis in women. The other risk factors are to have some type of immuno* suppressive illness, like HIV, AIDs, or diabetes mellitus [60]. Frequent Douching and wearing wet clothes for a long duration of time may also increase the risk [61].

3. DIAGNOSIS

Candidal vaginitis is mostly self-diagnosed. The clinical symptoms are the typical way to diagnose candidal vaginitis. The technical way for diagnosis requires microscopic examination of the vaginal discharge for the identification of yeast buds or yeast hyphae, which is most easily viewed in the wet mount with 10% KOH [62], it depends on the working microscope and the clinical experience of the provider and detects 40% to 70% of cases when compared to culture [63]. Sabouraud agar culture for vaginal discharge is considered the criterion standard for diagnosis, it is an expensive method and requires a long duration of time [64].

Recently the immunochromatographic method has been developed which is rapid screening tests to detect Candida infection within 30 minutes [65].

4. TREATMENT

The treatment depends on the frequency of the infections short-course vaginal therapy: an antifungal medication is taken for three to seven days which usually clears the infection. Antifungal medications are available as creams, ointments, and tablets, which include miconazole and terconazole.

- Single-dose oral medicine: a single dose of fluconazole (Diflucan) is an oral medication prescribed by the doctor, it is not recommended when one is pregnant.
- Long-course vaginal therapy: doctor prescribe an antifungal medication which is taken daily for a few weeks, followed by once a week for six months.
- Multidose oral medication: doctor prescribed two or more doses of an antifungal medication which is an oral medication for vaginal therapy, but is not recommended for pregnant women.
- Azole resistant therapy: boric acid, a capsule is inserted into the vagina. This medication can be fatal if taken orally and is used only to treat candida fungus which is resistant to the usual antifungal agents [66, 67].

IV. TRICHOMONIASIS

Trichomonas vaginalis is the most common, curable, non-viral sexually transmitted infection. It is caused by parasitic, pear-shaped, and motile protozoan, it adheres to the vaginal epithelium and releases cytotoxic substances that cause inflammation and breaks the epithelium [68]. Trichomonas vaginalis does not need cervical cells for growth like Chlamydia trachomatis and Neisseria gonorrhoeae, they are vaginal pathogens, and the whole vagina is at risk of being infected [69].

1. SYMPTOMS

- Pain during urination and intercourse
- Genital redness, burning, and itching
- A large amount of a thin vaginal discharge with a foul smell
- ❄♒♏ ❖♋♑♓■♋● discharge might be clear, white, gray, yellow, or green
- Discomfort over the lower stomach area [70, 71, 72]

2. RISK FACTOR

Lower education level, ethnicity, socioeconomic status, and douching are the risk factor for acquiring *Trichomonas vaginalis*, multiple sexual partners are also identified as risk factors [72].

3. DIAGNOSIS

The method used most often to diagnose trichomoniasis in the office setting has traditionally been a microscopic examination of saline wet mount for motile *trichomonas*, it has a

sensitivity of 50% to 60% when performed by experienced clinicians [73]. Recently developed methods for diagnosing trichomoniasis are Affirm VPIII (Maryland, Dickson, Sparks), the nucleic acid probe that evaluates for *Trichomonas vaginalis*, and in addition to the *Gardnerella vaginalis*. The sensitivity of these tests is 80% to 90%. OSOM and Trichomonas rapid test (Sekisui Diagnostics, Framingham, Massachusetts) are the rapid antigen test for trichomoniasis. If trichomonads are present then the vaginal collection swab will turn blue when it comes in contact with specific reagents [74]. It has a sensitivity rate of 83% to 90%. The result of Affirm VPIII is available within 45 minutes and OSOM Trichomonas rapid test takes 10 minutes to show the result [75].

4. TREATMENT

The only drug used for treating *Trichomonas vaginalis* are tinidazole and metronidazole [76]. The cure rate of tinidazole is 86% to 100%, whereas the cure rate of metronidazole is 90% to 95% only. Treatment is recommended for all the sex partners of women with trichomoniasis [77].

V. CONCLUSION

Vaginal infection is caused by different types of microorganism i.e. bacteria, fungi, protozoa, mycoplasma etc. Several risk factors are associated with it if not treated on time. Personal hygiene is one of the most crucial factor which girls should follow to avoid vaginal infection. Early signs and symptoms should not be avoided, the treatment should be started as soon as possible.

REFERENCES

1. Bachmann, G. A. & Nevadunsky, N. S. (2000, May 15). Diagnosis and treatment of atrophic vaginitis. American Family Physician, 61(10), 3090-3096.
2. http://www.aafp.org/afp/2000/0515/p3090.html
3. Nyirjesy, P. (2014, December). Management of persistent vaginitis. Obstetrics & Gynecology, 124(6), 1135-1146.
4. https://journals.lww.com/greenjournal/Abstract/2014/12000/Management_of_Persistent_Vaginitis.11.aspx.
5. Lobo RA, et al. Genital tract infections: Vulva, vagina, cervix, toxic shock syndrome, endometritis, and salpingitis. In: Comprehensive Gynecology. 7th ed. Philadelphia, Pa.: Elsevier; 2017. https://www.clinicalkey.com. Accessed Aug. 26, 2018.
6. Verhelst R, et al. (2004) Cloning of 16S rRNA genes amplified from normal and disturbed vaginal microflora suggests a strong association between Atopobium vaginae, Gardnerella vaginalis, and bacterial vaginosis. BMC Microbiol 4:16.
7. TL Charles, LA Meyn, MA Krohn, JG Lurie, SL Hillier, Association between the acquisition of herpes simplex virus type 2 in women and bacterial vaginosis. Clin Infect Dis 37, 319–325 (2003).
8. ER Boskey, RA Cone, KJ Whaley, TR Moench, Origins of vaginal acidity: High D/L lactate ratio is consistent with bacteria being the primary source. Hum Reprod 16, 1809–1813 (2001).
9. V Pybus, AB Onderdonk, Evidence for a commensal, symbiotic relationship between Gardnerella vaginalis and Prevotella bivia involving ammonia: Potential significance for bacterial vaginosis. J Infect Dis 175, 406–413 (1997).
10. Goldenberg, R. L., Culhane, J. F., Iams, J. D. & Romero, R. Epidemiology and causes of preterm birth. Lancet 371, 75–84 (2008).
11. Koparde, V. N., Parikh, H. I., Bradley, S. P. & Sheth, N. U. MEEPTOOLS: a maximum expected error based FASTQ read filtering and trimming toolkit. Int. J. Comput. Biol. Drug Des. 10, 237–247 (2017).
12. Nelson, D. B. et al. Early pregnancy changes in bacterial vaginosis-associated bacteria and preterm delivery. Paediatr. Perinat. Epidemiol .28, 88–96 (2014).
13. Callahan, B. J. et al. Replication and refinement of a vaginal microbial signature of preterm birth in two racially distinct cohorts of US women. Proc. Natl Acad. Sci. USA 114, 9966–9971 (2017).

14. Son, K.-A. et al. Prevalence of vaginal microorganisms among pregnant women according to trimester and association with preterm birth. Obstet. Gynecol. Sci. 61, 38–47 (2018).
15. Haque, M. M., Merchant, M., Kumar, P. N., Dutta, A. & Mande, S. S. First-trimester vaginal microbiome diversity: a potential indicator of preterm delivery risk. Sci. Rep. 7, 16145 (2017).
16. Ban, Y., An, L. & Jiang, H. Investigating microbial co-occurrence patterns based on metagenomic compositional data. Bioinforma 31, 3322–3329 (2015).
17. Witkin S.S. Mendes-Soares H. Linhares I.M. et al. Influence of vaginal bacteria and d- and l-lactic acid isomers on vaginal extracellular matrix metalloproteinase inducer: implications for protection against upper genital tract infections. MBio. 2013; 4https://doi.org/10.1128/mBio.00460-13vv.
18. O'Hanlon D.E. Moench T.R. Cone R.A.Vaginal pH and microbicidal lactic acid when lactobacilli dominate the microbiota.PLoS One. 2013; 8: e80074https://doi.org/10.1371/journal.pone.0080074
19. Fettweis J.M. Brooks J.P. Serrano M.G. et al.Differences in the vaginal microbiome in African American women versus women of European ancestry. Microbiology. 2014; https; https://doi.org/10.1099/mic.0.081034-0.
20. Zárate G. Nader-Macias M.E. Influence of probiotic vaginal lactobacilli on in vitro adhesion of urogenital pathogens to vaginal epithelial cells. Lett Appl Microbiol. 2006; 43: 174-180https://doi.org/10.1111/j.1472-765.2006.01934.x
21. Shi Y. Chen L. Tong J. et al. Preliminary characterization of vaginal microbiota in healthy Chinese women using cultivation-independent methods. J Obstet Gynaecol Res. 2009; 35: 525-532https://doi.org/10.1111/j.1447-0756.2008.00971.
22. Jaquiery A. Stylianopoulos A. Hogg G. et al. Vulvovaginitis: clinical features, aetiology, and microbiology of the genital tract. Arch Dis Child. 1999; 81: 64-67 .
23. Pabich W.L. Fihn S.D. Stamm W.E. et al. Prevalence and determinants of vaginal flora alterations in postmenopausal women. J Infect Dis. 2003; 188: 1054-1058https://doi.org/10.1086/378203
24. Genc M.R. Onderdonk A. Endogenous bacterial flora in pregnant women and the influence of maternal genetic variation. BJOG. 2011; 118: 154-163https://doi.org/10.1111/j.1471-0528.2010.02772.x .
25. Srinivasan S. Fredricks D.N. The human vaginal bacterial biota and bacterial vaginosis. Interdiscip Perspect Infect Dis. 2008; 2008: 750479 https://doi.org/10.1155/2008/750479.
26. Altizer, S. M., Nunn, C. L., Thrall, P. H., Gittleman, J. L., Antonovics, J., Cunningham, A. A., et al. (2003). Social organization and parasite risk in mammals: integrating theory and empirical studies. Annu. Rev. Ecol. Evol. Syst. 34, 517–547. doi:10.1146/annurev.ecolsys.34.030102.151725.
27. Graver, M. A., and Wade, J. J. (2011). The role of acidification in the inhibition of Neisseria gonorrhoeae by vaginal lactobacilli during anaerobic growth. Ann. Clin. Microbiol. Antimicrob. 10:8. doi: 10.1186/1476-0711-10-8
28. Thoma, M. E., Gray, R. H., Kiwanuka, N., Aluma, S., Wang, M. C., Sewankambo, N., et al. (2011a). Longitudinal changes in vaginal microbiota composition assessed by gram stain among never sexually active pre- and postmenarcheal adolescents in Rakai, Uganda. J. Pediatr. Adolesc. Gynecol. 24, 42–47. doi: 10.1016/j.jpag.2010.07.002
29. Uchihashi, M., Bergin, I. L., Bassis, C. M., Hashway, S. A., Chai, D., and Bell, J. D. (2015). Influence of age, reproductive cycling status, and menstruation on the vaginal microbiome in baboons (Papio anubis). Am. J. Primatol. 77, 563–578. doi:10.1002/ajp.22378.
30. Leitich, H., Bodner-Adler, B., Brunbauer, M., Kaider, A., Egarter, C., and Husslein, P. (2003). Bacterial vaginosis as a risk factor for preterm delivery: a meta-analysis. Am. J. Obstet. Gynecol. 189, 139–147. doi:10.1067/Mob.2003.339.
31. Mirmonsef, P., Hotton, A. L., Gilbert, D., Burgad, D., Landay, A., Weber, K. M., et al. (2014). Free glycogen in vaginal fluids is associated with Lactobacillus colonization and

low vaginal pH. PLoS ONE 9102467: doi: 10.1371/journal.pone.0102467.
32. Nauth, H. F., and Haas, M. (1985). Cytologic and histologic observations on the Sex-Hormone dependence of the Vulva. J. Reproduct. Med. 30, 667–674.
33. Spear, G. T., French, A. L., Gilbert, D., Zariffard, M. R., Mirmonsef, P., Sullivan, T. H., et al. (2014). Human alpha-amylase present in lower genital tract mucosal fluid processes glycogen to support vaginal colonization by Lactobacillus. J. Infect. Dis. 210, 1019–1028. doi: 10.1093/infdis/jiu231.
34. Gajer P, Brotman RM, Bai G, Sakamoto J, Schutte UM, et al. (2012) Temporal dynamics of the human vaginal microbiota. Sci Transl Med 4: 132ra52.
35. Zhou X, Brown CJ, Abdo Z, Davis CC, Hansmann MA, et al. (2007) Differences in the composition of vaginal microbial communities found in healthy Caucasian and black women. The ISME journal 1: 121–133.
36. Wilks M, Wiggins R, Whiley A, Hennessy E, Warwick S, et al. (2004) Identification and H2O2 production of vaginal lactobacilli from pregnant women at high risk of preterm birth and relation with outcome. J Clin Microbiol 42: 713–717.
37. Aagaard K, Riehle K, Ma J, Segata N, Mistretta TA, et al. (2012) A metagenomic approach to characterization of the vaginal microbiome signature in pregnancy. PLoS One 7: e36466.
38. Relman DA (2012) The human microbiome: ecosystem resilience and health. Nutr Rev 70: S2–9.
39. Hay PE, Lamont RF, Taylor-Robinson D, Morgan DJ, Ison C, Pearson J. Abnormal bacterial colonisation of the genital tract and subsequent preterm delivery and late miscarriage. BMJ 1994; 308: 295– 8.
40. Ralph SG, Rutherford AJ, Wilson JD.Influence of bacterial vaginosis on conception and miscarriage in the first trimester: cohort study. BMJ 1999; 319: 220– 3.
41. Martius J, Eschenbach DA. The role of bacterial vaginosis as a cause of amniotic fluid infection, chorioamnionitis, and prematurity – a review. Arch Gynecol Obstet 1990; 247: 1– 13.
42. Verhelst R, Verstraelen H, Claeys G, Verschraegen G, Delanghe J, Van SL, et al. Cloning of 16S rRNA genes amplified from normal and disturbed vaginal microflora suggests a strong association between Atopobium vaginae, Gardnerella vaginalis and bacterial vaginosis. BMC Microbiol 2004; 4: 16.
43. Fredricks DN, Fiedler TL, Marrazzo JM. Molecular identification of bacteria associated with bacterial vaginosis. N Engl J Med 2005; 353: 1899– 911.
44. Fredricks DN, Fiedler TL, Thomas KK, Oakley BB, Marrazzo JM. Targeted PCR for detection of vaginal bacteria associated with bacterial vaginosis. J Clin Microbiol 2007; 45: 3270– 6.
45. Collins MD, Wallbanks S. Comparative sequence analyses of the 16S rRNA genes of Lactobacillus minutus, Lactobacillus rimae and Streptococcus parvulus: proposal for the creation of a new genus Atopobium. FEMS Microbiol Lett 1992; 74: 235– 40.
46. Hauduroy P, Ehringer G, Urbain A, Guillot G, Magrou J. Dictionnaire des Bacteries Pathogenes. Paris: Masson, 1937.
47. Shukla SK, Meier PR, Mitchell PD, Frank DN, Reed KD. Leptotrichia amnionii sp. nov., a novel bacterium isolated from the amniotic fluid of a woman after intrauterine fetal demise. J Clin Microbiol 2002; 40: 3346– 9.
48. Geissdorfer W, Bohmer C, Pelz K, Schoerner C, Frobenius W, Bogdan C. Tuboovarian abscess caused by Atopobium vaginae following transvaginal oocyte recovery. J Clin Microbiol 2003; 41: 2788– 90.
49. Thomason JL, Gelbart SM, James JA, Edwards JM, Hamilton PR. Is analysis of vaginal secretions for volatile organic acids to detect bacterial vaginosis of any diagnostic value? Am J Obstet Gynecol 1988; 159:1509 –11.
50. Bradshaw CS, Morton AN, Hocking J, Garland SM, Morris MB, Moss LM, et al. months after oral metronidazole therapy and factors associated with recurrence High recurrence rates of bacterial vaginosis over the course of 12. J Infect Dis 2006; 193: 1478– 86.
51. Verstraelen H, Verhelst R, Claeys G, De BE, Temmerman M, Vaneechoutte M. Longitudinal analysis of the vaginal microflora

in pregnancy suggests that L. crispatus promotes the stability of the normal vaginal microflora and that L. gasseri and/ /or L. iners are more conducive to the occurrence of abnormal vaginal microflora. BMC Microbiol 2009; 9: 116.
52. Wayne LG, Brenner DJ, Colwell RR, Grimont PAD, Kandler O, et al. Report of the ad-hoc-committee on reconciliation of approaches to bacterial systematics. Int J Syst Bacteriol. 1987;37:463–4.
53. Jakobsson T, Forsum U. Changes in the predominant human Lactobacillus flora during in vitro fertilisation. Ann Clin Microbiol Antimicrob. 2008;7:14–21.
54. Schloss PD, Handelsman J. Status of the microbial census. Microbiol Mol Biol Rev. 2004;68:686–91.
55. Ravel J, Gajer P, Abdo Z, Schneider GM, Koenig SS, McCulle SL, Karlebach S, Gorle R, Russell J, Tacket CO, Brotman RM, Davis CC, Ault K, Peralta L, Forney LJ. Vaginal microbiome of reproductive-age women. Proc Natl Acad Sci U S A. 2011;108 Suppl 1:4680–7.
56. Bäckhed F, Ley RE, Sonnenburg JL, Peterson DA, Gordon JI.2005. Host-bacterial mutualism in the human intestine. Science 307:1915– 1920.
57. Bäckhed F, Ley RE, Sonnenburg JL, Peterson DA, Gordon JI.2005. Host-bacterial mutualism in the human intestine. Science 307:1915-1920.
58. Davies TJ, Pedersen AB. 2008. Phylogeny and geography predict pathogen community similarity in wild primates and humans. Proc R Soc Lond B Biol Sci 275: 1695– 1701.
59. Danielsson D, Teigen PK, Moi H. 2011. The genital econiche: focus on microbiota and bacterial vaginosis. Ann N Y Acad Sci 1230: 48– 48.
60. Galhardo CL, Soares JM, Simoes RS, Haidar MA, Rodrigues DLG, Baracat EC. 2006. Estrogen Estrogen effects on the vaginal pH, flora and cytology in late postmenopause after a long period without hormone therapy. Clin Exp Obstet Gynecol 33: 85– 89.
61. Keane FEA, Ison CA, Taylor-Robinson D. 1997. A longitudinal study of the vaginal flora over a menstrual cycle. Int J STD AIDS 8: 489– 494.
62. Kalyoussef S, Nieves E, Dinerman E, Carpenter C, Shankar V, Oh J, Burd B, Angeletti RH, Buckheit KW, Fredricks DN, Madan RP, Keller MJ, Herold BC. 2012. Lactobacillus proteins are associated with the bactericidal activity against E. coli of female genital tract secretions. PLoS One 7, e49506.
63. Martin HL, Richardson BA, Nyange PM, Lavreys L, Hillier SL, Chohan B, Mandaliya K, Ndinya-Achola JO, Bwayo J, Kreiss J.1999. Vaginal lactobacilli, microbial flora, and risk of human immunodeficiency virus type 1 and sexually transmitted disease acquisition. J Infect Dis 180: 1863– 1868.
64. Narushima S, Itoh K, Sankai T, Takasaka M, Otani I, Yoshikawa Y. 1997. Changes in normal vaginal flora of African green monkeys (Cercopithecus aethiops) during the menstrual cycle. Exp Anim 46: 47– 52.
65. Sewankambo N, Gray RH, Wawer MJ, Paxton L, McNairn D, Wabwire-Mangen F, Serwadda D, Li C, Kiwanuka N, Hillier SL, Rabe L, Gaydos CA, Quinn TC, Konde-Lule J.1997. HIV-1 infection associated with abnormal vaginal flora morphology and bacterial vaginosis. Lancet 350: 546– 550.
66. Street DA, Taylor-Robinson D, Hetherington CM. 1983. Infection of female squirrel monkeys (Saimiri sciureus) with trichomonas vaginalis as a model of trichomoniasis in women. Br J Vener Dis 59: 249– 254.
67. Turnbaugh PJ, Ley RE, Hamady M, Fraser-Liggett CM, Knight R, Gordon JI. 2007. The human microbiome project. Nature 449: 804-804– 810.
68. Weinstein L, Bogin M, Howard JH, Finkelsto -ne BB. 1936. A survey of the vaginal flora at various ages with special reference to the Doederline bacillus. Am J Obstet Gynecol 32: 211– 218.
69. Zhou X, Brotman RM, Gajer P, Abdo Z, Schüette U, M S, Ravel J, Forney LJ. 2010a. Recent advances in understanding the microbiology of the female reproductive tract and the causes of premature birth. Infect Dis Obstet Gynecol 2010: 737425.
70. Verstraelen H, Vervaet C, Remon J: Rationale and safety assessment of a novel intravaginal

drug-delivery system with sustained DL-lactic acid release, intended for long-term protection of the vaginal microbiome. PLoS One. 2016; 11(4):e0153441. 10.1371/journal.pone.0153441
71. Ventegodt S, Clausen B, Omar HA, et al.: Clinical holistic medicine: holistic sexology and acupressure through the vagina (Hippocratic pelvic massage). Scientific World Journal. 2006;6(2006):2066–79. 10.1100/tsw.2006.337
72. McMillan A, Dell M, Zellar MP, et al.: Disruption of urogenital biofilms by lactobacilli. Colloids Surf B Biointerfaces. 2011;86(1):58–64. 10.1016/j.colsurfb.2011.03.016
73. Collins SL, McMillan A, Seney S, et al.: Promising prebiotic candidate established by evaluation of lactitol, lactulose, raffinose, and oligofructose for maintenance of a Lactobacillus-Dominated vaginal microbiota. Appl Environ Microbiol. 2018;84(5):pii:e02200-17. 10.1128/AEM.02200-17
74. Gray RH, Kigozi G, Serwadda D, Makumbi F, Nalugoda F, Watya S, Moulton L, Chen MZ, Sewankambo NK, Kiwanuka N, Sempijja V, Lutalo T, Kagayii J, Wabwire-Mangen F, Ridzon R, Bacon M, Wawer MJ. 2009. The effects of male circumcision on female partners' genital tract symptoms and vaginal infections in a randomized trial in Rakai, Uganda. Am J Obstet Gynecol 200:42.e1.
75. Alcendor DJ. 2016. Evaluation of health disparity in bacterial vaginosis and the implications for HIV-1 acquisition in African American women. Am J Reprod Immunol 76:99–107
76. Turovskiy Y, Sutyak Noll K, Chikindas ML. 2011. The aetiology of bacterial vaginosis. J Appl Microbiol 110:1105–1128.
77. Mackelprang RD, Scoville CW, Cohen CR, Ondondo RO, Bigham AW, Celum C, Campbell MS, Essex M, Wald A, Kiarie J, Ronald A, Gray G, Lingappa JR, Partners in Prevention HSV/HIV Transmission Study Team. 2015. Toll-like receptor gene variants and bacterial vaginosis among HIV-1 infected and uninfected African women. Genes Immun 16:362–365.
78. Mitra A, Macintyre DA, Lee YS, Smith A, Marchesi JR, Lehne B, et al. Cervical intraepithelial neoplasia disease progression is associated with increased vaginal microbiome diversity. Sci Rep. 2015;5:16865.
79. Romero R, Hassan SS, Gajer P, Tarca AL, Fadrosh DW, Nikita L, et al. The composition and stability of the vaginal microbiota of normal pregnant women is different from that of non-pregnant women. Microbiome. 2014; 2(1):4.

Studies of Lipid Profile and Oxidative Stress Markers in Doxorubicin-Induced Cardio Toxicity in Rats Administered Adansonia Digitata Leaf Extract

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ABSTRACT

Cardiovascular disease is the world's leading cause of death. Lipoxidation plays a relevant role in the onset of cardiovascular diseases (CVD) causing about17 to 19 deaths annually. The usage of traditional drugs was influenced by the need for effective medications for the treatment of cardiovascular disease without side effects. The study aimed at investigating antilipidemic and antioxidative protection offered by Adansonia digitata leaf extract on doxorubicin-induced cardiotoxicity in wistar rats. Thirty male wistar rats were grouped into five of six (6) each:(1) normal control, received 0.5 mL of distilled water (2) received 20 mg/kg of DOX only (3) received 20 mg/kg of DOX +100 mg/kg of A. digitata leaf extract (4) received 20 mg/kg of DOX + 200 mg/kg of A. digitata leaf extract and (5) received 20 mg/kg of DOX+400 mg/kg of A. digitata DOX was administered subcutaneously weekly while extract was given orally/day for three weeks. Results revealed significant ($p>0.05$) increased in Troponin T, Creatinekinase and Lactate dehydrogenase in group2 against normal control. Reduction of these parameters was observed across the groups administered.

Keywords: lipid peroxidation; doxorubicin; cardiotoxicity; oxidative makers adnsonia digitata.

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ABSTRACT

Cardiovascular disease is the world's leading cause of death. Lipoxidation plays a relevant role in the onset of cardiovascular diseases (CVD) causing about17 to 19 deaths annually. The usage of traditional drugs was influenced by the need for effective medications for the treatment of cardiovascular disease without side effects. The study aimed at investigating antilipidemic and antioxidative protection offered by Adansonia digitata leaf extract on doxorubicin-induced cardiotoxicity in wistar rats. Thirty male wistar rats were grouped into five of six (6) each:(1) normal control, received 0.5 mL of distilled water (2) received 20 mg/kg of DOX only (3) received 20 mg/kg of DOX +100 mg/kg of A.digitata leaf extract (4) received 20 mg/kg of DOX + 200 mg/kg of A .digitata leaf extract and (5) received 20 mg/kg of DOX+400 mg/kg of A.digitata .DOX was administered subcutaneously weekly while extract was given orally/day for three weeks. Results revealed significant (p>0.05) increased in TroponinT, Creatinekinase and Lactate dehydrogenase in group2 against normal control. Reduction of these parameters was observed across the groups administered. A digitata extract. Elevation of MDA was recorded in group2 compared with normal control. This parameter decreased upon treated with the extract. Significant (p<0.05) reductions in Chol, TG, and LDL levels were obtained in group fed 400 mg/Kg b.wt of the extract in comparison with group 2 (DOX–induced only) and normal control. Significant variations of Chol, TG and LDL levels were observed within the text groups in dose dependent manner. HDL increased in all the text groups except group2.CAT and GPx activities decreased significantly (p>0.05) while SOD activity was non- significantly (p>0.05) decreased. Increase activities of these antioxidant enzymes were recorded across the test groups administered extract against group2 (DOX –induced only) and normal control. In this study A.digitata leaf extract has demonstrated its potential to delaying lipid peroxidation and protects oxidative damage induced by doxorubicin in the experimental rats.

Keywords: lipid peroxidation; doxorubicin; cardiotoxicity; oxidative makers adnsonia digitata.

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I. INTRODUCTION

The heart is distinctively prone to oxidative damage. Heart attack, also called myocardial infarction (MI), and related complications are the main causes of deaths throughout the world [1]. Doxorubicin (DOX) is one of the most efficient anticancer agents. The use of DOX in clinical setting is limited due to the extensive adverse effects. It is has been shown that 41% of cancer patients who received DOX are affected with various cardiac problem. DOX treatment increases the morbidity and mortality of cancer patients due to the heart failure [2]. Doxorubicin-induced cardiomyopathy is strongly linked to an increase in cardiac oxidative stress, as indicated by the depletion of endogenous antioxidant

enzymes, and accumulation of free radicals in the myocardium which increases the chance of DOX-induced cardiomyopathy [3].

Heart uses large amounts of fatty acids (FAs) as energy-providing substrates. Lipoxidation plays a relevant role in the onset of cardiovascular diseases (CVD), mainly in the atherosclerosis-based diseases in which oxidized lipids and their adducts have been extensively characterized and associated with several processes responsible for the onset and development of atherosclerosis, such as endothelial dysfunction and inflammation. More than 70% of all substrates used for ATP generation are derived from FAs, with the remaining sources being glucose, lactate, ketone bodies, and amino acids. The relatively tight coupling between lipid uptake and oxidation prevents accumulation of excess lipids in the cardiomyocyte. Several processes that affect heart function, including ischemia, sepsis, and heart failure, are associated with a reduction in FA oxidation (FAO) with a relative increase in anaerobic glycolysis and, in some cases, accumulation of nonoxidized FA derivatives in the form of lipids. In addition, excess circulating FA levels in type 2 diabetes mellitus and its precursor, the metabolic syndrome, also cause cardiac lipid accumulation.

Further investigations revealed that the correlation of high cholesterol with increased risk of cardiovascular events was related mainly to low-density lipoprotein (LDL)-cholesterol (LDL-C) [4,5]. In contrast, high-density lipo-protein (HDL-C) was shown to be inversely correlated to mortality from coronary heart disease [4, 5]. Based on these findings, the“cholesterol hypothesis was born, which proposed that LDL-C is causal for the development of atherosclerosis, and consequently, lowering of LDL-C would reduce the risk of myocardial infarction and other cardiovascular events.Compared to a healthy heart, lipid metabolism is altered in a stressed heart, with for example a reduced fatty acid β-oxidation in heart failure as well as during myocardial ischemia [6].

Andonsonia digitata (Baobab) plants are tropical trees, native to Africa, Australia and Madagascar but dispersed widely by humans. A. digitata is commonly found in the woodlands of African savannah, it is a very long-lived tree with multipurpose use. A. digitata contain glycosides, saponins, steroids and flavonoids while alkaloids, tannins and resins were not detected [7]. The medicinal property of A. digitata is based on some bioactive compounds that produce a definite physiological action on the human body, these chemical substances have a potential or established biological activity that has been identified and they are known as phytochemicals [8] There is, however, paucity of scientific evidence on antilipidemic properties of A.digitata leaf extract. As a result, the aim of the study was to determine lipid profiles and oxidative stress markers in doxorubicin-induced cardiac toxicity in rats administered Adansonia digitata extract.

II. MATERIAL AND METHODS

2.1 Plants materials

Plant material Fresh leaves of A.gigitata were collected from Kaduna State, Northern part of Nigeria. The leaves obtained were carefully rinsed under running water, dried under room temperature (250C) in the laboratory. It was milled and weighed before extraction.

2.2 Assay kits and Chemicals

Most of the chemical materials utilized in the study came from Sigma Chemicals Co. (St Louis, Mo, USA). Doxorubicin was obtained from Pfizer Global Pharmaceutical Limited in Nigeria. Assay kits for Creatinekinase, Superoxide dismutase (SOD), Catalase (CAT), Glutathione peroxidise (GPX), Lactate dehydrogenase (LDH) were purchased from Randox Laboratories Ltd, Co-Atrim, United Kingdom. Troponin T research kit was supplied by Glory Science co ltd, www.glorybio.com.

2.3 Experimental animals

Thirty (30) male wistar rats (mean weight 105±0.35g) were ordered from the animal house of Department of Zoology and Environmental Science, University of Nigeria, Nsukka. Rats were housed using clean iron cages under standard

environmental conditions of temperature (24± 10C) and relative humidity (45-50%) under a 12 h dark-light cycle. Acclimatization of the rats took 7 days before dosing and allowed free access to drinking water and standard pellets feed. The research protocols were approved by the Animal Ethics Committee, College of Natural Science, Michael Okpara University of Agriculture, Abia State, Nigeria. The approval was in line with the Guide for the Care and Use of Laboratory Animals.

2.4 Preparation of extract

A milled 500 g plant material was extracted in 2.0 L ethanol for 72 h at 300C on an orbital shaker (Stuart Scientific Orbital Shaker, UK) at room temperature. This was centrifuged at 1500 rpm for 5 min and the filtrate further filtered with wahtman No 4 filter paper. It was concentrated using rotary evaporator at 400C and the yield was 21.60 g. Reconstitution of the sample in distilled water was done to give the required concentrations of, 100, 200 and 400 mg /Kg body weight used in the study

2.5 Design of Experimental

A total of thirty male wistar rats were grouped into five of six (6) each:(1) Normal control, received 0.5 mL of distilled water (2) received 20 mg/kg of DOX only (3) received 20 mg/kg of DOX +100 mg/kg of A.digitata leaf extract (4) received 20 mg/kg of DOX + 200 mg/kg of A .digitata leaf extract and (5) received 20 mg/kg of DOX+400 mg/kg of A. digitata DOX was administered subcutaneously weekly while extract was given orally for three weeks.

2.6 Biochemical Analysis

2.6.1 Cardiac biochemical marker assessment

Methods described by Wurzburg et al. [9] and Szasz et al. [10] were used to determine the activity of creatine kinase (CK). Lactate dehydrogenase (LDH) activity was determined using the Witt and Trendelenburg method.

2.6.2 Assessment of Oxidative stress marker

The activity of superoxide dismutase (SOD) in the heart was measured using Misra and Fridovich's [11] method, which was later modified by Kakkar et al. The activity of catalase was determined using the Aebi method [12].] The level of lipid peroxidation as malondialdehyde (MDA) was determined using the Varshey and Kale principle [13].

2.6.3 Determination of lipids profile

Determination of lipids profile (HDL, LDL. TG and Cholesterol) was strictly by established laboratory methods.

2.6 Preparation of serum and tissues

Rats were sacrificed under anaesthesia by cervical dislocation. The blood sample was aseptically collected through cardiac puncture and transferred into sample labeled bottles, while the heart was still beating. Whole blood was used for enzyme assays while other part was allowed to stand for 2 hours to perfect clotting and centrifuged (model SM800B, Surgifriend Medicals, Essex, England) at 1000 rpm. Sera were removed with Pasteur pipette for determination of other parameters. Rats were quickly dissected and their heart were excised and transferred into ice-cold 0.25 M sucrose solution for histopathological examination.

2.7 Histopathological evaluation

Heart tissues were fixed in buffered 10% formalin and processed for histopathological examination as described by Abdel-Raheem [14]. Briefly, four micrometer-thick paraffin sections were prepared and stained with haematoxylin and eosin for light microscope examination by pathologist.

2.8 Statistical Analysis

Data collected were analysed using one-way analysis of variance (ANOVA). Level of significance was used to assess significant difference between the control and treated group at $p<0.05$. Results were expressed as mean ±SEM.

III. RESULT

Cardiac markers; Troponin T, Creatinekinase and Lactate dehydrogenase were determine.

Doxorubicin caused significant myocardial damage, resulting in a significant ($p<0.05$) increase in TroponinT level and increased activities of Creatine Kinase and Lactate dehydrogenase in group 2 as against the test groups and normal control. (Fig.1, 2 and 3). Significant ($p<0.05$) decrease of creatine kinase and LDH concen- tration were observed in groups received 400 mg/Kg of the extract (Fig. 2 and Fig.3) compared with other groups administered 100 and 200 mg/ Kg b.wt of the extract respectively. Similar observation was made in CAT and GPx activities where SOD activity demonstrated nonsignificant ($p>0.05$) decreased. Increase activities of these antioxidant enzymes were recorded across the test groups against group 2(DOX –induced only). Elevation of MDA was recorded (Fig.7) in group2 compared with other groups. Dose dependent decrease in MDA was observed in group 3, 4 and 5 which received 200, 300 and 400 mg/Kg b.wt of A.digitata respectively. Lipid profile was determined. Significant ($p<0.05$) reduction in cholesterol, TG, and LDL as shown in Fig. 8, 9 and 11 levels were obtained in group fed 400 mg/Kg b.wt of the extract in comparison with group 2 (DOX–induced only) and Group1 (Normal control). Significant variations of Chol, TG and LDL levels were observed within the text groups in dose dependent manner. Marked increase of HDL concentration was obtained in all the text groups which received treatment as against the rats induced with doxorubicin only (Fig. 7). Further more, 400 mg/Kg treatment recorded significant ($p<0.05$) increase of HDL level compared with other test groups.

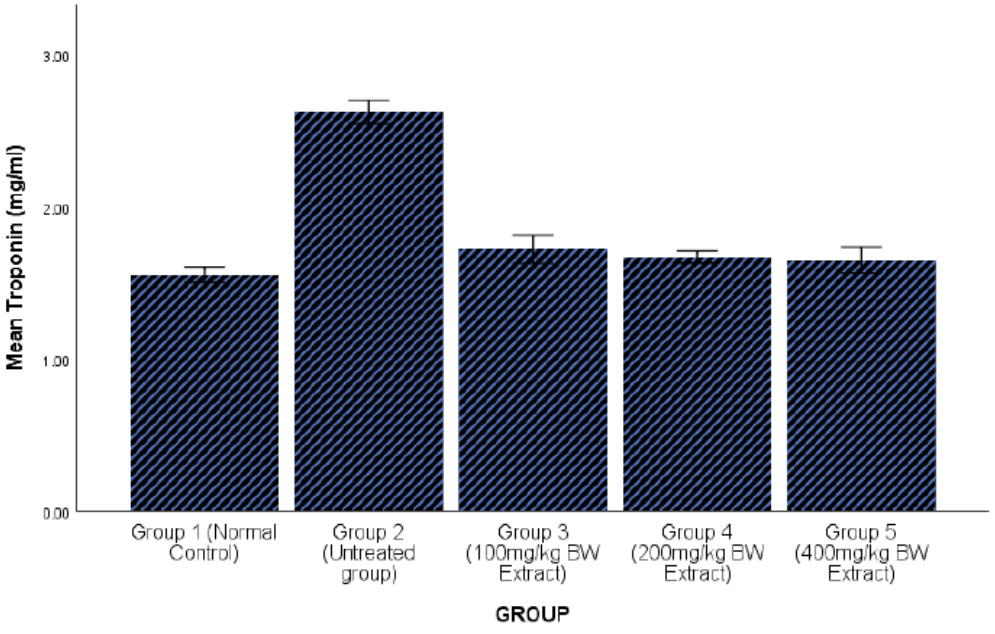

Fig. 1: Troponin level (mmol/L) of DOX- induced male wistar rats administered methanol leaf extracts of A.digitata. Values are mean of 6 determination (n=6)

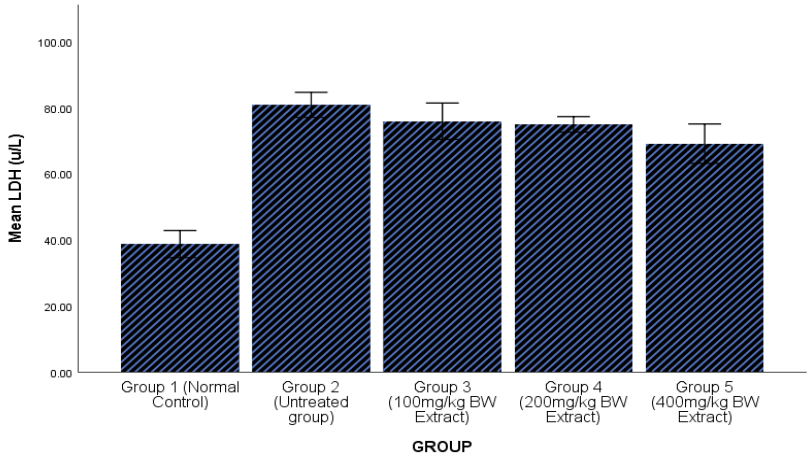

Fig.2. LDH (u/L) concentration of DOX- induced male wistar rats administered methanol leaf extracts of A. digitata. Values are mean of 6 determination (n=6)

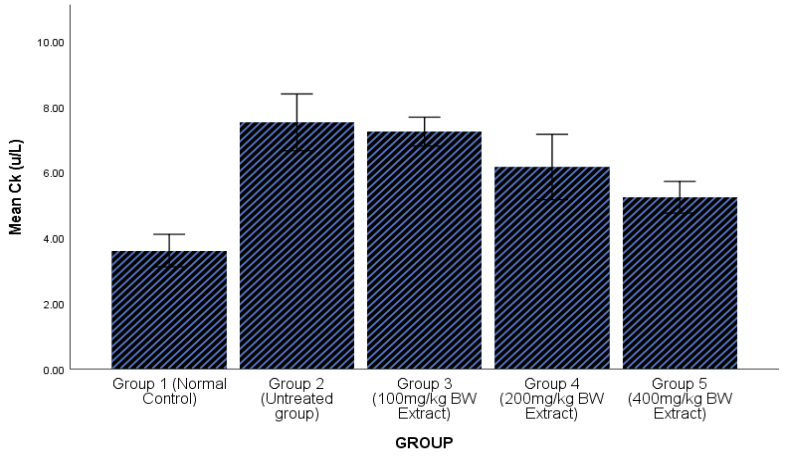

Fig. 3: Ck (u/L) level of DOX- induced male wistar rats administered methanol leaf extracts of A. digitata. Values are mean of 6 determination (n=6)

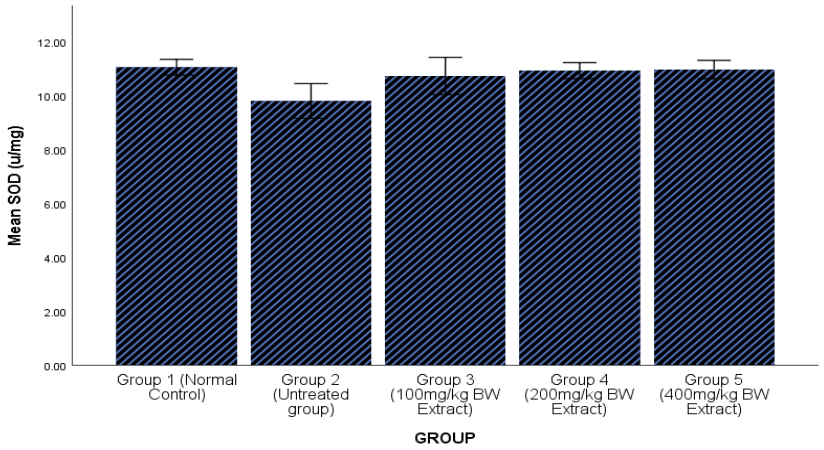

Fig. 4: SOD (u/mg) activity of DOX- induced male wistar rats administered methanol leaf extracts of A. digitata. Values are mean of 6 determination (n=6)

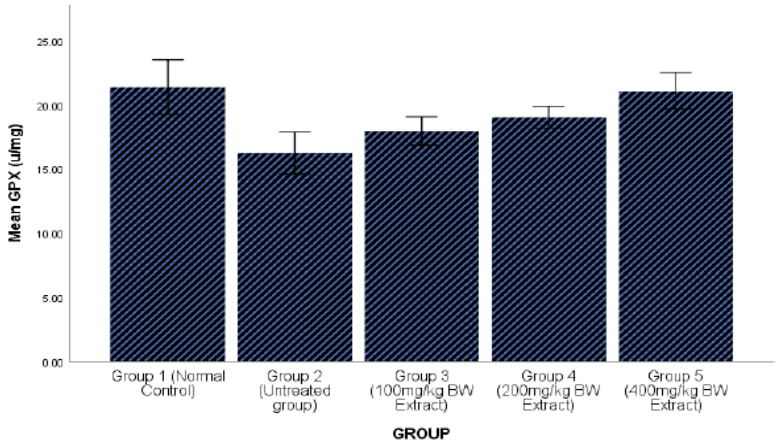

Fig. 5: GPX (u/mg) activity of DOX- induced male wistar rats administered methanol leaf extracts of A. digitata. Values are mean of 6 determination (n=6)

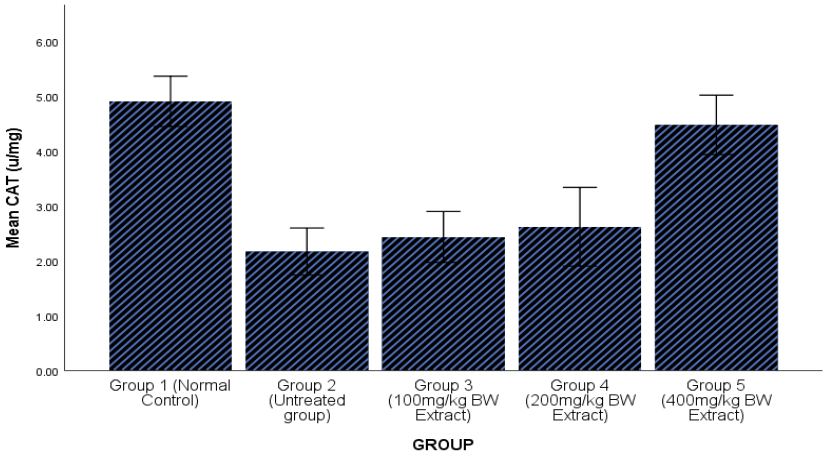

Fig. 6: CAT (u/mg) activity DOX- induced male wistar rats administered methanol leaf extracts of A. digitata. Values are mean of 6 determination (n=6)

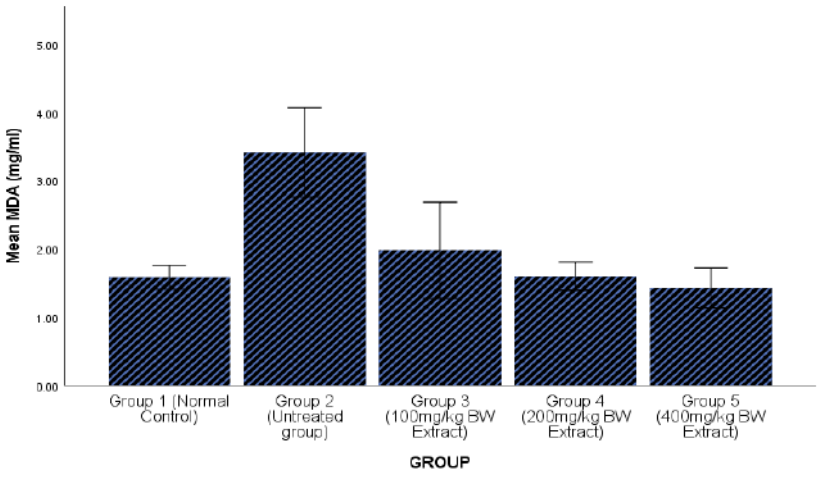

Fig. 7: MDA (mg/ml) concentration of DOX- induced male wistar rats administered methanol leaf extracts of A.digitata. Values are mean of 6 determination (n=6)

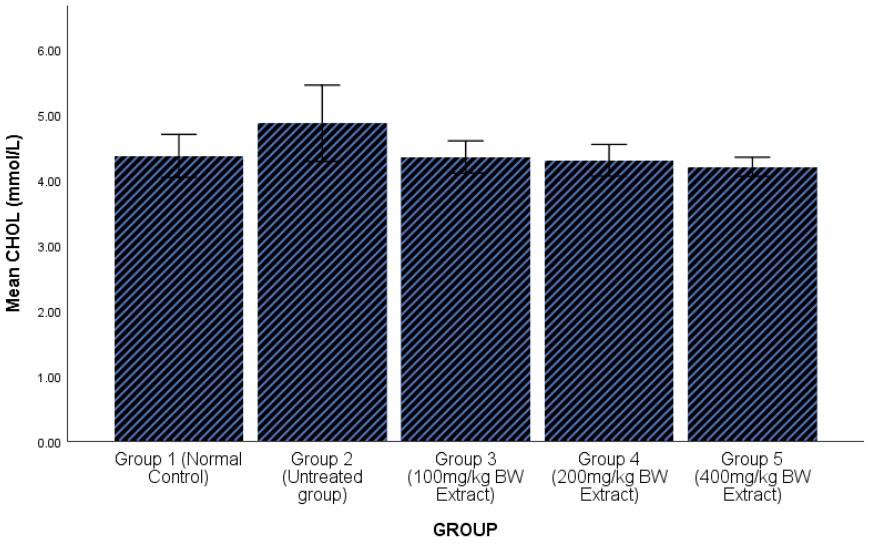

Fig. 8: Cholesterol (mmol/L) concentration of DOX- induced male wistar rats administered methanol leaf extracts of A.digitata. Values are mean of 6 determination (n=6)

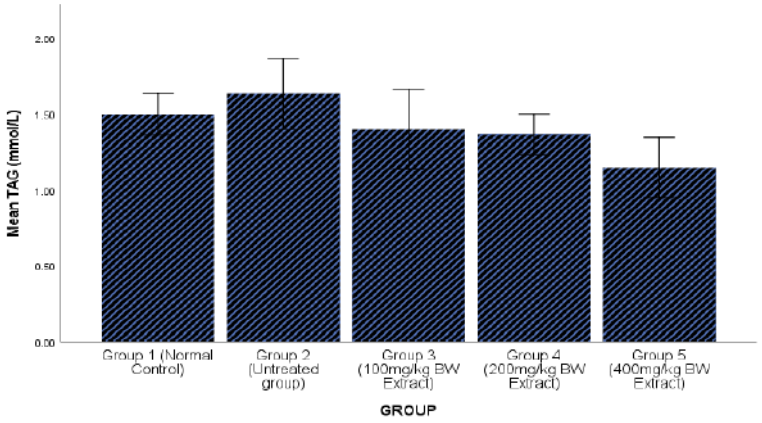

Fig. 9: TAG (mmol/L) Concentration of DOX- induced male wistar rats administered methanol leaf extracts of A. digitata. Values are mean of 6 determination (n=6)

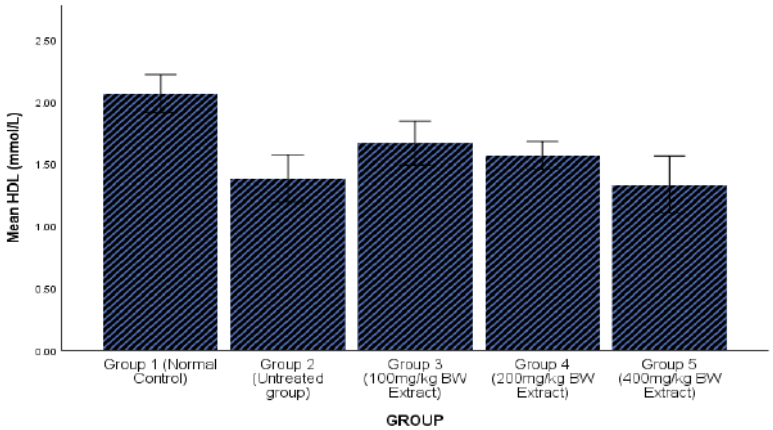

Fig. 9: HDL (mmol/L) concentration of DOX- induced male wistar rats administered methanol leaf extracts of A. digitata. Values are mean of 6 determination (n=6)

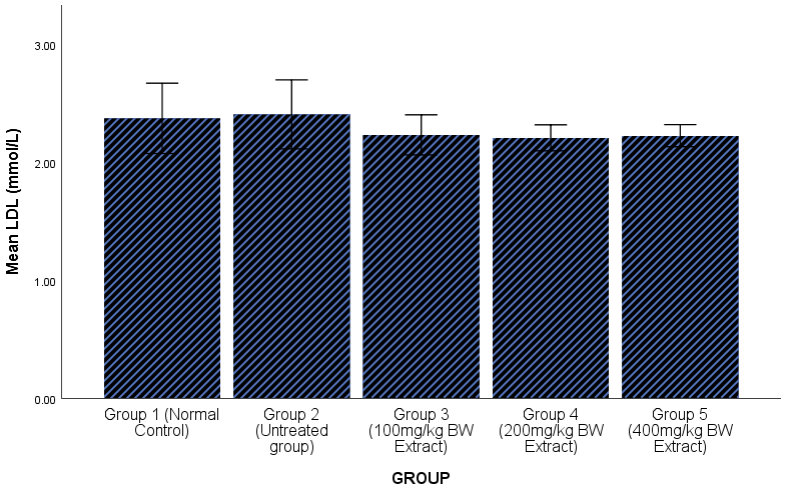

Fig. 10: LDL (mmol/L) concentration of DOX- induced male wistar rats administered methanol leaf extracts of A. digitata. Values are mean of 6 determination (n=6)

IV. DISCUSSION

The heart is distinctively proper to oxidative damage. Depletion of endogenous antioxidants facilitates oxidative stress in DOX–induced cardiomypathy. Accumulation of free radicals in the myocardium increases the chance of DOX-induced cardiomyopathy [3]. Heart uses large amounts of fatty acids (FAs) as energy-providing substrate. Oxidation of lipid plays an important role in the onset of cardiovascular diseases (CVD), especially in the atherosclerosis-based diseases in which oxidized lipids and their adducts have been extensively characterized and associated with several processes responsible for the onset and development of atherosclerosis, such as endothelial dysfunction and inflammation.

Cardiac markers; Troponin T, Creatine kinase and Lactate dehydrogenase were determined. Result revealed a significant ($p<0.05$) increase in TroponinT level and increase activities of creatinekinase and Lactate dehydrogenase in group 2 as against the test groups and normal control. However, administration of A.digitata extract reduced the concentration of these markers indicating repair mechanism offered by the extract. This could be attributed to viable bioactive constituents present in the plant extract.

The bioactive agents from natural sources have gained fundamental importance in modern system of medicines, reducing the risks of cardiac ailments by scavenging the free radicals formation [15]. These natural medicinal plants exert protective therapeutic effect through a series of processes, including the inhibition, modulation, and regulation of the expression of various proteins such as contractile and structural proteins, and glycoproteins, regulating the calcium levels and improvement in the functioning of mitochondria [16].

Oxidative stress plays major role in DOX-induced cardiotoxicity by generation of lipid peroxidation. Myocardial tissue is prone to free radical damage due to fewer amounts of antioxidants like SOD and CAT present in the heart [18, 19]. Administration of DOX at cumulative dose (20 mg/kg) increases the lipid peroxidation and depletion of the endogenous antioxidants in the myocardium. Similar biochemical changes have been reported by several other studies [17, 18].

High levels of serum triglycerides help mark conditions that are associated with increased risk for CHD and peripheral atherosclerosis. High triglycerides are associated with increased risk for Coronary Artery Disease (CAD) in patients with other risk factors, such as low HDL-cholesterol.

Consequently, elevated levels of cholesterol increase the risk for coronary heart disease (CHD). Cholesterol is measured to help assess the

patient's risk status and to follow the progress of patient's treatment to lower serum cholesterol concentrations. In this study, statistical significant decrease in some lipids parameters was obtained followed with increase in HDL especially at 400 mg/Kg b.wt administration of A. digitata, The ability of the extract to ameliorate the lipids abnormality is due to, partly phytoconstituents (phenolic compound, flavonoids, saponin, and many more) and inhibitory activity to lipid synthesis. Stimulation of HMGCoA-reductase activity by insulin was proposed to be blocked by the extracts, although other insulin-dependent phenomena may not be influenced. These results suggest an indirect modulation of hydroxy-methylglutaryl-CoA-reductase activity as the most likely inhibitory mechanism of the A. digitata extracts.

Decrease in MDA in all the text groups was recorded when compared with the DOX-induced only. A.digitata, based on this finding could delay or inhibits lipidoxidation. The extent of the extract to counteract the free radicals that could abstract electron (s) from the unsaturated lipids molecule by donating its electron is the most predictable mechanism. Pre-treatment with A. digitata extract significantly ($p>0.05$) reduced the elevated level of malondialdehyde across the test groups and much effect was observed in group4 administered with 400 mg/kg b. wt. The result was in agreement with the report Ogunleye et al., [19], Ebaid et al., [20] and Olayemi et al., [21].

V. CONCLUSION

Methanol extract of Adansonia digitata alleviated lipids abnormalities and oxidative stress induced by doxorubicin as shown by improved oxidative stress biomarkers. Finally, it was observed that leaf extract of Adansonia digitata shielded rats from doxorubicin-induced myocardial injury in dose dependent manner.

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Conflict of interest

Authors declare non existing conflict of interest

REFERENCES

1. Roger VL. (2007). Epidemiology of myocardial infarction. Med Clin N Am. 2007; 91(4):537–552.
2. Ragavendran, P., Sophia, D Arulraj, A and V. K. Gopalakrishnan, " Cardioprotective effect of aqueous, ethanol and aqueous ethanol extract of Aerva lanata (Linn.) against doxorubicin induced cardiomyopathy in rats," Asian Pacific Journal of Tropical Biomedicine, vol.2, supplement 1, pp. S212–S218, 2012. View at: Google Scholar.
3. Octavia, Y., Tocchetti, C.G., Gabrielson, K.L Janssens, S., Crijns, H.J and Moens, A.L (2012) "Doxorubicin-induced cardiomyopathy : from molecular mechanisms to therapeutic strategies," Journal of Molecular and Cell- ular Cardiology, vol. 52, no. 6, pp. 1213–1225, View at: Publisher Site | Google Scholar.
4. Gordon, T., Castelli, W.P., Hjortland, M., Kannel, W.B and Dawber, T.R (1977). High-density li-poprotein as a protective factor against coronary heart-disease-Framingham Study, Am. J. Med. 62 (1977) 707–714.
5. Kannel, W.B, Castelli, W.P. and Gordon, T (1979) Cholesterol in the prediction of atherosclerotic disease. New perspectives based on the Framingham study, Ann. Intern. Med. 90: 85–91.
6. Lopaschuk, G, D Ussher, J.R. Folmes, C.D, Jaswal, J.S and Stanley, W.C (2010). Myo-cardial fattyacid metabolism in health and disease, Physiol. Rev. 90: 207–258.
7. Chukwuma CO, Fatima A, Nurudden O, Alonge O, and Onyinye F, Nwgbara I (2017). Phytochemical, Elemental and proximate analyses of stored sun-dried and shade dried Baobab (Adansonia digitata) leaves. Preprint Converting enzyme inhibitors and angiotensin II receptor blockers on all cause, mortality cardiovascular deaths and cardiovascular

events in patients with diabetes mellitus: Ameta analyses. JAMA internal medicine 17 4(5):773-785.
8. Sinija VR, Mishra HN (2008). Green tea: Health benefits .Journal of Natural and Environmental Medicine 17(4):232-242.
9. Szasz G, Gerhard W, Gruber W. Creatinine kinase in serum; 5. Effect of trial on isoenzyme activity during storage at various temperatures. Clin. Chem. 1978;24(9):1557-1563.
10. Wurzburg U, Hennrich N, Lang H, Prellwitz W, Neumeier D, Kendel M. Determination of creatinine kinase - MB in serum using inhibition antibodies. Klin. Wochenschr. 1976;54(8):357-360
11. Misra HP, Fridovich I. The role of superoxide anion in the autoxidation of epinephrine and a simple assay for superoxide dismutase. J. Biol. Chem. 1972;247(10):3170-3175.
12. Aebi H. Catalase In; Methods of enzymatic analysis. Ed. By Hu Bergmeyer, Chemic Academic Press Inc Verlog. 1974; 2:673- 685.
13. Varshey Rand Kale RK. Effect of calmodulin antagonist on radiation induced lipid peroxidation in microsomes. Int. J. Rad. Biol. 1990;58:733-743.
14. Abdel-Raheem IT, Abdel-Ghany AA.(2009) Hesperidin alleviates doxorubicin-induced cardiotoxicity in rats. J Egypt Natl Canc Inst. 21:175–84.
15. Wang L, Li Y, Deng W, et al. Cardio-protection of ultrafine granular powder for Salvia miltio rrhiza Bunge against myocardial infarction. J Ethnopharmacol. 2018; 222:99–106. [Pub Med] [Google Scholar].
16. Ali Shah, S.M., Akram , M., Riaz, M., Munir, N. and Rasool.,G (2019) Cardioprotective Potential of Plant-Derived Molecules: A Scientific and Medicinal Approach Dose Response: 2019 Apr-Jun; 17(2).
17. Puri A, Maulik SK, Ray R, Bhatnagar V. Electrocardiographic and biochemical evidence for the cardioprotective effect of vitamin E in doxorubicin-induced acute cardiotoxicity in rats. European Journal of Pediatric Surgery. 2005;15 (6):387–391. [Pub Med] [Google Scholar].
18. Xin Y, Zhou G, Deng Z, et al. Protective effect of Lycium barbarum on doxorubicin-induced cardiotoxicity. Phytotherapy Research. 2007; 21(11):1020–1024. [PubMed] [Google Scholar.
19. Ogunleye, O.O., Jatau, I., Natala A. J. and Ola-Fadunsin, S.D (2020) Effects of aqueous extract of fruit pulp of Adansonia digitata L. on the oxidative stress profile against Trypanosoma brucei infection in albino rats. Clinical Phytoscience, 6:57.
20. Ebaid H, Bashandy SAE, Alhazza IM, Hassan I, Al-Tamimi J. Efficacy of a methanolic extract of Adansonia digitata leaf in alleviating hyperglycemia, and oxidative stress of diabetic rats. Biomed Res Int.
21. Olayemi., A.A., David, K.B., Adeoye, S.W., Ajoke, O.E Akinpelu, A.T4 and Akinloye, O.M (2021) Doxorubicin-(Induced Cardio Toxicity in Albino Rats Protected by Adansonia Digitata (Baobab) Leaf Extract. Annual Research & Review in Biology: 36(7): 12-22.

Literature Review on the General Health of Young People and Adolescentes and Reports from Health Professionals on the Impact of COVID-19 on this Population

Arthur Galvão Rodrigues Costa, Bianca Dore Soares Guedes, Maria Motta Nogueira & Mariana Pereira Augusto Maciel

ABSTRACT

Introdução: A adolescência e juventude é uma época marcada por mudanças físicas, biológicas e psicossociais, as quais implicam na necessidade de vivenciar novas experiências e aprendizados, analisando tópicos a respeito da saúde, sexualidade e questões sociais. As Diretrizes de Atenção Integral de Saúde de Adolescentes e Jovens visam o fortalecimento da prevenção e promoção da saúde para esse grupo prioritário, por meio da reorientação dos serviços de saúde a fim de favorecer a eficácia das respostas da assistência à saúde aos adolescentes e jovens. Objetivo: O presente artigo tem a finalidade de abordar diversos aspectos, os quais podem ser relativos à saúde, convívio familiar, aprendizagem, sexualidade e outros, que trazem impacto na vida do adolescente.

Keywords: adolescent health; youth health; health promotion at school.

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Literature Review on the General Health of Young People and Adolescentes and Reports from Health Professionals on the Impact of COVID-19 on this Population

Revisão bibliográfica acerca da saúde geral do jovem e do adolescente e relato de profissionais da saúde sobre o impacto do COVID-19 nesta população

Arthur Galvão Rodrigues Costa[α], Bianca Dore Soares Guedes[σ], Maria Motta Nogueira[ρ] & Mariana Pereira Augusto Maciel[Ↄ]

RESUMO

Introdução: A adolescência e juventude é uma época marcada por mudanças físicas, biológicas e psicossociais, as quais implicam na necessidade de vivenciar novas experiências e aprendizados, analisando tópicos a respeito da saúde, sexualidade e questões sociais. As Diretrizes de Atenção Integral de Saúde de Adolescentes e Jovens visam o fortalecimento da prevenção e promoção da saúde para esse grupo prioritário, por meio da reorientação dos serviços de saúde a fim de favorecer a eficácia das respostas da assistência à saúde aos adolescentes e jovens. Objetivo: O presente artigo tem a finalidade de abordar diversos aspectos, os quais podem ser relativos à saúde, convívio familiar, aprendizagem, sexualidade e outros, que trazem impacto na vida do adolescente.

Reflexão crítica: Os temas abordados, como os problemas relacionados à sexualidade, gravidez na adolescência, álcool e outras drogas, bullying, saúde mental, comorbidades e nutrição são de importante significância no aperfeiçoamento das abordagens na Atenção Integral de Saúde de Adolescentes e Jovens, visando atender as necessidades dessa população de forma integral e equitativa.

Conclusão: Conclui-se que, a saúde do adolescente e do jovem é um campo da área da saúde bastante significativo e de extrema importância, pois como foi visto, envolve diversos fatores com alta influência no decorrer de seu ciclo de vida.

Palavras-chave: saúde do adolescente; saúde do jovem; promoção de saúde na escola.

Keywords: adolescent health; youth health; health promotion at school.

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I. INTRODUÇÃO

A adolescência e juventude é uma época marcada por mudanças físicas, biológicas e psicossociais, o que provoca nos indivíduos a necessidade de buscar novos hábitos, experiências e aprendizado para se entender e entender o mundo em que vivem. Analisando essas mudanças, um dos tópicos principais é o entendimento a respeito da saúde, descobrir, quem, onde e como pode os ajudar conhecer e compreender mais sobre essa temática. (SUASSUNA *et al.*, 2020)

Diante dessa perspectiva da busca por conhecimento e autoconhecimento, destaca-se alguns pontos, como, a sexualidade, que é um incentivo a autonomia dos adolescentes e jovens. Nota-se que a maioria dos jovens, atualmente, possuem conhecimento sobre as doenças sexualmente transmissíveis (DSTs) e a gravidez na

adolescência, contudo, continuam se expondo constantemente a esses riscos em razão da falta de diálogo com seus responsáveis e na escola, local que os jovens passam maior parte do tempo, evidenciando a necessidade da intervenção tanto da família quanto da escola. A escola apresenta papel fundamental na saúde dos jovens, por esse motivo que o Programa Saúde na Escola (PSE), uma política pública que objetiva a melhoria da saúde dos adolescentes e jovens na rede escolar pública é tão importante. A partir das ações que o PSE promove de promoção e prevenção de saúde, com a ajuda do incentivo dos profissionais e participação dos estudantes, o aprendizado sobre a saúde do jovem se expande, o colocando como protagonista. (MONTEIRO *et al.*, 2019)

Nesse contexto, abordar a saúde do adolescente requer uma interpretação sobre as diferentes formas de viver a adolescência e de viver a vida. Portanto, implica em uma dinâmica de repensar as atividades de saúde e de educação em saúde, as quais se voltam para essa parcela significativa da população, os adolescentes. No âmbito das políticas socioeconômicas do Brasil, a esfera da saúde e educação em saúde pública não abrange as singularidades e necessidades dos adolescentes, não atingindo de forma satisfatória a grande massa da população (FERREIRA *et al.,* 2007).

As repercussões dessa deficiência na atenção à saúde do adolescente e jovem estão presentes no estilo de vida adotado por eles. A exemplo disso, observa-se a entrada precoce no mercado de trabalho, muitas vezes, em condições de exploração da força de trabalho e extensas cargas horárias, se dá em razão das condições socioeconômicas familiares e necessidade financeira. Em virtude disso, muitos jovens e adolescentes se iniciam na prostituição, em ambientes de crime e violência, envolvimento com drogas e álcool e, na maioria das vezes, entram no processo de evasão escolar (FERREIRA *et al., 2007).*

As Diretrizes de Atenção Integral de Saúde de Adolescentes e Jovens visam o fortalecimento da prevenção e promoção da saúde para esse grupo prioritário, por meio da reorientação dos serviços de saúde a fim de favorecer a competência e eficácia das respostas da assistência à saúde aos adolescentes e jovens. Dessa forma, enfatiza-se a necessidade de intervenções intersetoriais e interdisciplinares, com o objetivo de fomentar a participação juvenil nas iniciativas dos serviços de saúde, fazendo parte do planejamento, execução e avaliação das ações de saúde que afetam seu bem-estar e favorecer o exercício da cidadania dos adolescentes e jovens (BRASIL, 2010).

II. REFLEXÃO CRÍTICA

2.1 Sexualidade e gravidez na adolescência:

O despertar da sexualidade e sua atividade sexual inicia-se em idade cada vez mais precoce dentro da população atual de adolescentes e jovens, aliada a esta vivência sexual prematura, observa-se a ocorrência crescente de gestações nesta fase da vida, fato que tem sido identificado como um dos grandes problemas de saúde pública, tanto no Brasil quanto em muitos países (TORRES *et al.*, 2018).

Nesse contexto, faz-se necessário entender essa fase do ciclo de vida para além das mudanças biológicas e psicológicas, considerando que a introdução no âmbito social e a cultura modelam a vivência dessa fase. Dessa forma, as adolescentes que passam por essa experiência se tornam capazes de conciliar os cuidados à saúde e a escolaridade junto à maternidade a partir de uma orientação e apoio, evidenciando o papel essencial exercido pelo profissional de saúde, que tem o objetivo de contribuir com as inseguranças encontradas neste período. Observou-se também, que os fatores os quais contribuem para a gravidez na adolescência são falta de perspectiva de vida, baixa autoestima, más condições de educação e saúde, falta de lazer, ingenuidade, submissão, violência, desinformação e expectativas de mudança de status social, assim como, a falta de utilização de métodos contraceptivos (CREMONESE, 2019; TORRES *et al.*, 2018).

Em virtude do processo de gestação e maternidade, existem questões sociais que podem ser desencadeadas, trazendo dificuldades a esse processo, tais como: as situações de pobreza, de monoparentalidade por abandono do parceiro,

isolamento social, baixa autoestima, evasão escolar e desemprego. Verifica-se que esses problemas podem repercutir em riscos pessoais para o desenvolvimento de ambos. Diante disso, observa-se que há um despreparo dos profissionais de saúde quanto ao acolhimento das adolescentes, ademais, as ações de promoção que objetivam construção de ambientes favoráveis à prevenção da gravidez na adolescência são insuficientes (CREMONESE, 2019).

Ademais, a maternidade em uma idade prematura pode resultar em evasão escolar, piores qualificações no trabalho e consequentemente piores empregos, que levam à perpetuação do ciclo de pobreza. Apesar de ser exigido o amadurecimento forçado dessas mulheres, elas continuam a ter os desejos de sua idade, como terminar a escola a fim de prover um futuro melhor para seu filho. Dessa forma, deve haver uma melhor organização na saúde para um melhor acompanhamento e acolhimento, contando com equipe multiprofissional, a fim de proporcionar qualidade na assistência à saúde dos adolescentes (TORRES *et al.*, 2018).

Segundo os enfermeiros, a sexualidade é um dos assuntos que incentiva a autonomia individual dos adolescentes, e diante disso, é necessário que estes recebam as devidas orientações para auxiliar na tomada de decisões, baseados em informações claras, considerando seu contexto, para que consiga desfrutar da sua sexualidade com segurança. Notou-se que na atualidade, em sua maioria, os jovens possuem o conhecimento dos riscos das DSTs e da gravidez, contudo, as suas exposições a esses riscos continuam constantes. Com isso, torna-se perceptível a necessidade não apenas da teoria dentro das escolas e universidades acerca destes temas recorrentes, mas primordialmente das ações educativas em saúde, que através de dinâmicas, problematizações e formas práticas, possam promover a reflexão, discernimento e por fim a conscientização acerca da prevenção necessária a estes riscos. (BESERRA, *et al.* 2017; SEHNEM, *et al.*, 2019)

Sendo assim, é na escola que os adolescentes e jovens passam maior parte de seu tempo, local onde se iniciam os primeiros relacionamentos amorosos, e em razão disso, os programas educativos devem ser realizados nesse espaço, visando a tomada de decisões e a melhoria de habilidades, de prevenção e promoção em saúde, como ações educativas com abordagens problematizadoras, nas quais seja permitida a identificação própria em cada situação apresentada. Para que, por consequência, a escola comece a representar um local de reunião para a expressão de comportamentos, troca de informações e esclarecimento de dúvidas sobre uma vida sexual e reprodutiva saudável. (MONTEIRO, *et al.*, 2019; SEHNEM, *et al.*, 2019).

2.2 Uso de drogas lícitas/ilícitas e álcool

O uso de drogas ilícitas, como o crack, e outras drogas por adolescentes implica, inicialmente, em repercussões sociais, principalmente, relacionadas à problemas no relacionamento familiar, visto que por serem as pessoas mais próximas ao usuário, precisam lidar com a situação. Dessa forma, verifica-se que no ambiente familiar de usuários adolescentes, é muito comum a existência de conflitos, discussões e separações e até mesmo violência, o que resulta na fragilidade do vínculo entre o adolescente e sua família (PAULA; JORGE; VASCONCELOS, 2019).

Ademais, notou-se redução do consumo de álcool e cigarro e aumento do uso de drogas ilícitas dentre as últimas gerações de adolescentes e jovens. Salienta-se também que em contraste a diminuição do consumo de cigarro, o uso de outros produtos do tabaco está em crescimento, especialmente o narguilé´, o que deve ser monitorado com bastante atenção. Estudos revelam que a maior chance de experimentação do tabaco ocorre na adolescência. Portanto, prevenir e retardar a iniciação desse hábito é um grande desafio para a saúde pública, tornando-se prioritário o desenvolvimento de políticas para essa faixa etária (OLIVEIRA-CAMPOS *et al.*, 2018).

Além da conscientização constante sobre o uso de drogas abordado nas ações educativas dentro de escolas e universidades, também é importante

promover a reflexão de jovens em tratamento desse uso dentro de comunidades terapêuticas, compartilhando suas experiências e aumentando a compreensão e restauração do ser subjetivo entre eles. Foi visto que o início do uso foi estimulado pela curiosidade, amigos e familiares, muitas vezes pela falta da criticidade acerca do tema, principalmente o da dependência. Isso revela a necessidade da aproximação das ações e profissionais envolvidos com a realidade dos jovens, para assim compreender e formular a ação, sobretudo com resolutividade para estas situações vividas, abordando de maneira dinâmica nas ações. Com isso, o suporte é dado não apenas aos usuários de drogas, mas aos jovens em geral, e consequentemente, suas famílias. (SOUZA PINTO *et al.*, 2017).

Outra problemática é que em razão da falta de identificação dos estudantes com os educadores, podendo vir de déficits educacionais, dificuldades pedagógicas, problemas na comunidade e diferenças de renda, a aproximação dos profissionais com os adolescentes e jovens adultos se torna prejudicada, dificultando o diálogo, elaboração e execução de projetos de prevenção do uso de drogas. Desse modo, poucos entendem as consequências do uso de drogas, que podem variar de reprovações e evasão escolar, estresse e até violência. Reforçando a necessidade da identificação dos jovens dentro das situações abordadas nas ações educativas, priorizando a metodologia problematizadora, mas também, haja vista que a família desempenha um papel essencial na formação do indivíduo, faz-se necessário reafirmar a importância dos laços familiares no cuidado com os usuários, e que além disso, a família, quando amparada por uma rede de apoio satisfatória, é o principal suporte para os adolescentes. (PAULA; JORGE; VASCONCELOS, 2019; SANDIM, *et al.*, 2020)

2.3 Bullying

O *bullying* é uma violência intencional e repetitiva, praticada por uma pessoa e especificamente dirigida a outra, expressando uma relação de desigualdade e poder, é um problema generalizado em todas as escolas de todo o mundo. O *bullying,* exerce um efeito negativo sobre várias áreas da vida da pessoa afetada, tais como: a escolarização, a saúde e o desenvolvimento psicossocial, atingindo, além de suas vítimas, a família destas. As agressões, geralmente, são manifestadas de forma reativa, como defesa contra alguma provocação ou agressão sofrida, mas também podem se apresentar de forma proativa, como uma ação proposital e elaborada, com o intuito de atingir algo ou alguém (SILVA *et al.,* 2019).

Os adolescentes vítimas de *bullying* usualmente se sentem impossibilitados de pedir ajuda, seja por acharem que se trata de uma brincadeira, mesmo que estejam em intenso sofrimento, por carência de informação a respeito, pela vergonha de não poder resolver a situação sozinhos, por presumirem que sua rede de suporte não conseguirá ajudá-los, por medo de retaliação dos agressores, dentre outras possibilidades que os enclausuram num experienciar tomado pela dor, podendo durar semanas ou até´ anos (PIGOZI, 2018).

O cuidado a estas vítimas devem ser de modo integral e subjetivo, levando em consideração a sua rotina, lar e não apenas o ambiente de estudo, envolvendo todas as possíveis relações. Através da divulgação de cartilhas e ambientes de diálogo, foi possível discutir acerca da violência vivida entre as demais experiências, levando a orientações benéficas como o autocuidado e redes de auxílio à saúde mental, confirmando que há pouco cuidado quanto a prática de *bullying* dentro das instituições, necessitando das ações de educação em saúde, abordando o tema, assim como o subjetivo, singular de cada indivíduo, cultura de paz, respeito às diferenças e equidade (PIGOZI, 2018).

Nas escolas, faz-se extremamente necessária a instituição de medidas destinadas ao enfrentamento do *bullying,* com o objetivo de que a agressão, tanto verbal quanto não verbal, não seja normalizada nas relações escolares**.** Na perspectiva da diminuição da prática da saúde mental, física e desempenho escolar marcada pela violência escolar característica do bullying, existe a intervenção do Teatro do Oprimido, que tem como objetivo romper a dicotomia entre o teatro e

a plateia, assim abre espaço para os adolescentes se abrirem com os outros e relatar situações vivenciadas, ocorrendo o enfrentamento do bullying e a melhoria da qualidade de vida dos adolescentes no ambiente escolar (ALENCASTRO, *et al.,* 2020; SILVA *et al.,* 2019)

2.4 Comorbidades e nutrição

A adolescência se caracteriza como uma fase em que as pessoas tornam-se mais sujeitas aos apelos dos grupos sociais em que se inserem ou até à mudança do estilo de vida, as questões referentes ao desenvolvimento socioeconômico da região onde vivem, também influenciam na relação com os hábitos alimentares. Com efeito disso, grande parte dos fatores de risco para as doenças crônicas não transmissíveis inicia-se na adolescência e pode influenciar a saúde a curto e a longo prazo, sendo o ambiente escolar um importante território para a promoção da saúde, visto que há uma concentração desse público nesses espaços. Além disso, aspectos socioeconômicos, tais como: renda familiar, nível educacional, convivência familiar com os pares e na escola, residir com os pais, e aspectos como sexo e idade, podem impactar o nível de saúde dessa faixa etária.

No Brasil em 2009, por ação do Ministério de Saúde em parceria com o Ministério da Educação e o Instituto Brasileiro de Geografia e Estatística (IBGE) foi implantada a Pesquisa Nacional de Saúde do Escolar (PeNSE), que tem o objetivo de avaliar e monitorar os aspectos da saúde das crianças e adolescentes dentro das escolas, fornecendo, assim, informações aos gestores e profissionais de saúde para a elaboração de políticas de saúde específicas para adolescentes, ocorre trienalmente e está na sua terceira edição. Com efeito disso, ao comparar as três edições da PeNSE nas capitais brasileiras, visto que em 2016, cerca de 20,3 milhões de adolescentes frequentavam a escola, verificou-se redução consistente no consumo de alimentos não saudáveis, como refrigerantes e guloseimas. No que se refere a alimentos saudáveis, houve redução no consumo regular de feijão e discreto aumento na ingestão regular de frutas. Ocorreu diminuição no consumo de álcool e cigarros, mas viu-se aumento expressivo na experimentação de drogas ilícitas e na estabilidade do percentual de alunos que praticam atividades físicas. (BALBINO; BARBOZA, 2019; OLIVEIRA-CAMPOS *et al.*, 2018; LEAL *et al.,* 2019).

É evidente que as práticas de marketing social das empresas alimentícias na promoção de seus produtos impactam significativamente no estilo de vida e nos hábitos alimentares, principalmente, dos adolescentes. O consumo desses produtos com baixo valor nutritivo e potencial efeito negativo sobre a saúde se torna favorável em função de sua praticidade e fácil preparo, e seu consumo é estimulado através do incentivo dos pais, da atratividade do produto, do fácil acesso, da pressão social e da conveniência. De acordo com pesquisas, as principais motivações acerca da escolha de tal comportamento alimentar se relacionam com: a dificuldade de acesso à alimentação saudável, falta de interesse dos jovens, o sabor dos alimentos gordurosos, a diferença de preço e o incentivo da família. (BALBINO; BARBOZA, 2019).

Dessa forma, o marketing se faz como uma estratégia eficaz para a promoção da mudança de comportamento do indivíduo, podendo colaborar com a redução do consumo de bebidas açucaradas, as quais aumentam o risco de diabetes tipo 1 e obesidade, por meio da reeducação alimentar e conscientização dos riscos decorrentes de uma má alimentação. Ademais, verifica-se o papel dos hábitos alimentares no desenvolvimento de doenças crônicas não transmissíveis (DCNT), tais como: problemas cardiovasculares como doença coronariana e insuficiência cardíaca, câncer, diabetes e doenças respiratórias e renais crônicas. Além disso, sabe-se que os hábitos de vida têm uma significativa influência na saúde dos adolescentes e atualmente, com a prevalência de comportamentos sedentários, a obesidade e sobrepeso, o maior tempo dedicado aos comportamentos sedentários, o maior tempo de uso de aparelhos eletrônicos e o maior consumo de alimentos ultraprocessados influenciam negativamente a situação de saúde dos adolescentes e, consequentemente, sua qualidade de vida. Nesse contexto, é importante incentivar a realização de intervenções por meio da exposição

de informações calóricas das bebidas açucaradas e outros alimentos gordurosos, possibilitando o acesso à informação. (BALBINO; BARBOZA, 2019; LEAL *et al.,* 2019).

Nos Estados Unidos foi observado aumento da prevalência de consumo de frutas e vegetais entre 2002 e 2010; o mesmo se deu também no Brasil para adultos, pela presença de muitas evidências do benefício do consumo de frutas e hortaliças na proteção contra doenças cardiovasculares, câncer, entre outras. Entretanto, esse consumo foi baixo entre os adolescentes, resultado que não difere de outras pesquisas, como o Health Behavior in School-aged Children (HSBC), na Europa, que mostrou 36% de consumo de frutas aos 13 anos e 31% aos 15 (OLIVEIRA-CAMPOS *et al.*, 2018).

Outrossim, como comorbidade bastante presente entre pesquisas utilizadas para estudo, a asma constitui uma das principais causas de internação hospitalar, no entanto, é considerada uma condição sensível à Atenção Primária à Saúde. Nesse contexto, a PeNSE 2015, incorporou questões relacionadas à asma ativa a fim de orientar futuras políticas de saúde que contribuam para a redução do número de casos no país. A alta prevalência de sintomas de asma nos últimos 12 meses (23,52%) e de relato de asma no passado (17,92%) entre escolares da nona série do ensino fundamental confirmam a importância da asma como problema de saúde entre adolescentes brasileiros, e destaca o Brasil entre os países com mais altas prevalências de asma do mundo. (RIBEIRO-SILVA *et al.*, 2018).

Além disso, atualmente, uma das questões mais levantadas nos meios das redes sociais é referente ao padrão de beleza. Em busca do padrão estético de beleza corporal, que se constitui de magreza e juventude, as desordens alimentares apresentam-se como uma das consequências da busca frenética pelo corpo perfeito, colocando em segundo plano a saúde mental e fisiológica. Essas desordens fazem parte de um grupo de transtornos mentais que podem ser fatais, entre esses, destacam-se a anorexia nervosa e a bulimia nervosa. Esses transtornos atingem principalmente adolescentes e adultos jovens do sexo feminino, podendo resultar em severos danos biológicos, psicológicos e odontológicos (CHIMBINHA *et al., 2019).*

Com a análise da literatura produzida envolvendo programas de intervenção em escolas com alto índice de obesidade e sedentarismo, foi visto que o estímulo semanal, por volta de 3 dias, com exercícios aeróbicos em atividades físicas por volta de 12 semanas foi efetivo, contudo, pouco aderido por outras instituições. O resultado trouxe inúmeros benefícios, principalmente quanto à composição corporal e postura, comprovando ser uma das estratégias de abordagem com excelentes resultados, que pode ser utilizada para diminuição dessa comorbidade em específico, por atingir exatamente o hábito do sedentarismo e o combater. (TORNQUIST *et al.*, 2016).

Com isso, compreender os comportamentos que levam a exposição de risco do desenvolvimento de comorbidades é essencial entre jovens e adolescentes, além da investigação de quais são os riscos mais presentes nessa etapa do desenvolvimento, contudo, deve-se distinguir que o jovem não pode ser apenas associado ao desenvolver de uma doença, mas em sua integralidade, facilitando o processo. Foi possível analisar o efeito de ações educativas da Estratégia Saúde da Família (ESF) em comportamentos de risco à saúde entre um grupo de adolescentes. Notou-se que, sempre há uma baixa participação nas ações, principalmente quando se tratava do consumo de álcool e outras drogas, alimentação adequada, atividade sexual desprotegida, sedentarismo, diminuindo a potencialidade das ações pela falta de adesão, sendo necessárias estratégias de abordagem mais diversificadas e fluidas, para provocar maior participação, análise de dificuldades e uma conscientização efetiva. (CHIMELI, *et al.*, 2016; RAIZEL, *et al.*, 2016).

2.5 Programas educativos em saúde

O Programa Saúde na Escola (PSE) é uma política intersetorial brasileira, instituída em 2007, resultado da parceria entre o Ministério da Saúde e o Ministério da Educação, objetivando a melhoria da saúde dos escolares da rede pública de ensino, com ações de promoção, prevenção e

atenção à saúde. As escolas participantes do PSE devem incluir em seu projeto político pedagógico os temas das atividades em saúde desenvolvidas, os quais devem ser debatidos em sala de aula pelos professores, assessorados pelos profissionais de saúde das Unidades Básicas de Saúde de referência (critério de proximidade), com agendas programadas para esse fim (OLIVEIRA *et al.*, 2018).

Para realização de ações educativas para jovens e adolescentes, se faz necessário um estudo, que aumente os resultados através do combate de todas as dificuldades que possam vir a acontecer. É primordial o uso do método problematizador, possibilitando o diálogo e a escuta informal, fixando melhor o conhecimento através de uma metodologia ativa, revezando entre tópicos que direcionam a discussão. Pode-se utilizar de objetos que ao serem passados em rodas de conversa, jogos e dinâmicas, utilizando o método de perguntas e resposta, com base na necessidade epidemiológica do território, além de visitas a espaços de aprendizagem que podem ser estimuladoras para os estudantes, como feiras de ciência, museus e até mesmo os serviços de saúde. (SILVA FERREIRA *et al.*, 2016).

2.6 Vacinação, promoção e prevenção à saúde

Habitualmente, os adultos cuidam-se voluntariamente. Os bebês, as crianças, os idosos, os enfermos e os deficientes necessitam de cuidado ou assistência completa nas atividades de autocuidado. Por sua vez, os adolescentes mantêm -se no limbo, ora se cuidam voluntariamente, ora precisam de supervisão e comando para as atividades de autocuidado. A adolescência é uma fase da vida propícia a problematizar sobre hábitos de vida, nesse período, eles se encontram mais propícios ao aprendizado. Contudo, devido ao desconhe- cimento de atividades de promoção e prevenção de saúde e pouco vínculo com profissionais de saúde, os estudantes percebem a importância da informação em suas vidas, e estão dispostos a buscar e participar de atividades que possibilitem a redução da vulnerabilidade (BORGES *et al.*, 2019; SUASSUNA *et al.*, 2020).

Logo, exercem um papel essencial na tomada de decisões relacionadas à saúde. A decisão sobre tomar a vacina ou não, por exemplo, pode ser influenciada por diversos aspectos. Entre eles, o mais importante está relacionado à circulação das informações, pela internet, televisão, rádios e jornais. Mesmo as vacinas sendo disponibilizadas pela rede pública, grande parte dos adolescentes apresenta o cartão de vacinação atrasado, seja pelo esquecimento, em virtude das longas filas, pela falta de conhecimento ou falta de tempo (VIEGAS *et al.,* 2019).

No Brasil, os adolescentes estão entre os grupos prioritários para o Programa Nacional de Imunização, isso se deve à alta suscetibilidade a algumas doenças preveníveis por meio da vacinação, e, principalmente, pela baixa cobertura vacinal dessa faixa etária. Entretanto, no âmbito da saúde, sabe-se que ainda existem falhas nas práticas de cuidados destinados aos adolescentes, o que explica a baixa resolutividade das singularidades dessa faixa etária. Desse modo, a insatisfatória demanda de adolescentes nas Unidades de Saúde da Família, a baixa taxa de adesão aos programas e ações desenvolvidas e a resistência à vacinação, são considerados fatores que impedem alcançar o objetivo de cobertura vacinal entre os adolescentes. Desse modo, destaca-se a importância de uma comunicação efetiva e a disseminação de informações corretas sobre a relevância de se vacinar por parte dos profissionais de Atenção Primária à saúde (APS). Além disso, tal comunicação contribui para o fortalecimento do vínculo e se torna um incentivo à população para o acesso aos serviços de saúde (VIEGAS *et al.,* 2019).

A compreensão dos adolescentes do sexo masculino em relação ao cuidado com sua saúde, pode passar despercebida devido a fatores como contexto social, com isso, para estimular práticas de autocuidado, torna-se necessário a fomentação de um ambiente para os adolescentes falarem livremente sobre suas inquietações, dúvidas, motivações e expectativas, para que a partir disso, ele se sinta protagonista na prática do autocuidado (CARVALHO, *et al.,* 2019).

Nesse contexto, o Programa de Saúde na Escola (PSE) foi criado, com o intuito de reforçar a saúde dos escolares, contribuindo com a promoção e

atenção à saúde, a prevenção de riscos e agravos e com o enfrentamento da vulnerabilidade que as crianças e adolescentes da rede pública de ensino encaram. Ademais, a partir desse programa, a relação e integração entre os segmentos da Saúde e Educação pode se estabelecer. Entre os componentes do PSE, estão: o monitoramento e avaliação da saúde dos estudantes, monitorando a situação vacinal e de doenças (VIEGAS *et al.*, 2019).

Através da escuta e participação ativa na rotina de adolescentes e jovens adultos, foi possível pontuar que existe um déficit na percepção de unidades básicas de saúde como meio de promoção e prevenção. Logo, pode-se levantar problemáticas decorrentes desse bloqueio por esta parcela da população, visto que é necessária uma aproximação com o público-alvo em ações específicas de promoção de saúde para obter resultados, de forma que a atenção seja integral e longitudinal, atingindo as vulnerabilidades. Sugestões como associação a organizações não governamentais (ONGs) locais, que levam em consideração a experiência e vivência dos jovens, podem ser praticadas na tentativa de gerar um vínculo, diálogo e o atendimento, garantidos na Atenção Integral à Saúde de Adolescentes e Jovens na Promoção, Proteção e Recuperação da Saúde. (ANHAS, CASTRO-SILVA, 2017; BRASIL, 2010)

O estímulo à prática de atividades físicas é uma ferramenta importante na promoção à saúde, principalmente associada à informação sobre a necessidade e suas repercussões na saúde, assim como formas e locais de prática. Dentro das universidades, foi possível perceber que entre os universitários, a partir dos dois primeiros anos, houve uma diminuição de praticantes de esportes e adesão a academias físicas, consequente da falta de tempo, espaço ou capacitação no âmbito de cuidados à saúde. Com isso, o risco de desenvolver comorbidades, como discutido anteriormente, aumenta drasticamente dentro destas instituições, necessitando de intervenções, podendo ser das mais diversas formas. Portanto, é reforçada a necessidade do reconhecimento do déficit antes de promover a ação educativa, pois se assim for feito, as chaves de efetividade são melhores, aumentando o bem-estar entre os estudantes. (OLIVEIRA, DORFIA, QUADROS, 2017).

2.7 Saúde do adolescente na pandemia da COVID-19

Em tempos de COVID-19 a saúde mental dos adolescentes foi grandemente afetada, assim ocorreu uma prevalência de sintomas depressivos e de ansiedade, bem como a combinação desses sintomas. Assim, a situação pandêmica provocou irritabilidade e medo, além das mudanças provocadas pela puberdade, abalando a saúde mental do adolescente. Outro fator que foi agravado, com início de medidas de distanciamento social, foi o aumento da vulnerabilidade de adolescentes em contexto de violência doméstica, já que precisaram passar mais tempo em suas casas, precisando ficar mais tempo próximos de figuras parentais abusivas que utilizam de castigos físicos ou práticas de punição para controlar atitudes indesejadas dos adolescentes. (OLIVEIRA, *et al.*,2019)

Com o decorrer da pandemia do coronavírus, as fragilidades do Sistema Único de Saúde - SUS, impossibilitando a real consolidação do SUS. Considerando esse cenário a população adolescente, mesmo apresentando Planos de Contingência Municipais, a falta de ações socioeducativas e a ausência de profissionais como médico e/ ou enfermeiro nessas ações, fica inviável a efetivação do enfrentamento do coronavírus. (OLIVEIRA, 2020)

III. RELATO DA ENTREVISTA

No primeiro relato, conta-se com a contribuição da cirurgiã-dentista e professora do módulo de Atenção à Saúde na Faculdade de Ciências Médicas da Paraíba, Luisiane de Avila Silva. Em suas experiências no campo da saúde do adolescente e do jovem, Luisiane conta que participou de rodas de conversas do Programa Saúde na Escola com adolescentes e jovens, que tratavam de temas variados além daqueles relativos à saúde bucal, tais como a cultura da paz, o *bullying* e respeito. Além disso, a profissional participou de atividades realizadas em

ambulatórios de HIV, AIDS e outras DSTs na Unidade de Saúde da Família, que tinham o objetivo de propagar informações a respeito da DST, suas formas de contágio e tratamento. Em relação às dificuldades trazidas pelo cenário pandêmico atual, verifica-se a imposição de uma barreira quanto à realização de tais atividades, visto que o distanciamento social, nesse momento, deve ser priorizado. Dessa forma, nota-se a necessidade de adaptação das ações de saúde para que a promoção da mesma seja viabilizada. Os meios de comunicação online, rádios que circulam na comunidade e as redes sociais são importantes recursos que contribuem para a divulgação de informações essenciais.

No segundo relato, descreve-se as experiências da psicoterapeuta e orientadora vocacional, graduada em Psicologia, Joseane Feitosa Barnabé. Em relação à saúde mental do jovem e adolescente, percebe-se que essa fase é um momento crucial na vida de todas as pessoas, onde vivências de tomada de decisão, adaptações à vida adulta, expectativas e pressão dos pais e familiares são marcantes. Na adolescência, a interação e convívio rotineiro com os colegas se faz muito importante, e é nesse aspecto, que a pandemia do covid-19 mais tem afetado e dificultado a vida dos adolescentes e jovens. Nesse contexto, o acolhimento e a escuta entre os grupos de iguais ficam prejudicados, além disso, o sentimento de frustração em relação ao futuro, estudos e a vida torna-se mais latente, assim como, a ansiedade. Ademais, o relacionamento familiar tem significativa influência na saúde mental da maioria dos adolescentes, assim sendo, dentro de caso deve-se priorizar um convívio saudável e leve, onde todos se sintam confortáveis, Portanto, existem algumas maneiras que auxiliam a contornar essa situação e ajudar os jovens e adolescentes, tais como: o incentivo ao autoconhecimento, autopercepção, cuidado consigo mesmo, procurar formas de melhorar seu estilo de vida, traçar metas a curto prazo, prática de exercícios físicos e outros.

No terceiro relato, há um foco na sexualidade e gravidez na adolescência, informado pela enfermeira obstetra Carol Vasconcelos. A ativista em saúde das mulheres, relata que gestantes mais jovens já são bastantes comuns na maternidade, mas ainda há casos que chocam os profissionais de saúde, como gestantes de 12 anos ou de 15 anos, já na segunda gestação. Assim, com um ou dois anos do primeiro parto, geralmente, há outra gestação, percebe-se a recorrência de mães adolescentes, sendo um dado alarmante e necessitando de intervenção para minimizar a situação. Nesse contexto, as repercussões sociais - como o ciclo de pobreza e baixa escolaridade - e saúde emocional e física - tais como aborto, aporte nutricional e parto prematuro - têm grande foco, devendo ser trabalhado. Além disso, os impactos da COVID-19 mostraram que durante o isolamento social aumentaram-se os casos de violência doméstica, assim como dificuldade no acesso a métodos contraceptivos e, consequentemente, o aumento de gestantes adolescentes vítimas de violência sexual, repercutindo físico e psiquicamente na vida dessas jovens. Logo, as ações educativas sobre o assunto já são bastante complicadas e durante o período em que se vive, houve uma piora, sendo necessário uma articulação entre família, assistência social e equipe multiprofissional. Acredita-se que o trabalho deve vir não só para os adolescentes, mas principalmente para a família, a fim de que exista uma educação combinada. Por fim, buscar falar sobre métodos contraceptivos e sexualidade, não é incentivar o início da vida sexual, mas sim, informar e educar, para quando decidirem iniciar, estarem orientados positivamente. Como no distanciamento social, não há como existir rodas de conversas, deve-se incentivar as escolas a utilizar vídeos informativos e aplicativos mediados pelos meios de saúde, mantendo a orientação desses jovens. Ademais, deve-se normalizar a ida dos adolescentes à UBS, assim como, incentivar o exame preventivo para essas adolescentes e garantia de métodos contraceptivos em UBS e escolas.

Por fim, no quarto relato, o ponto central é a atenção básica na educação sexual e métodos contraceptivos na adolescência, sob a perspectiva de Gioconda Maria da Silva Mendonça, farmacêutica pós-graduada em Saúde Pública, Judicialização de medicamentos, farmácia clínica e gestão pública. A entrevistada relata que, apesar

do ministério da saúde considerar adolescentes, pessoas na faixa entre 15 e 18 anos, porém atualmente, o início da vida sexual começa mais cedo, principalmente em municípios pequenos, onde ela possui mais experiência. Em razão disso, o Brasil é o país com maior número de adolescentes grávidas na américa latina. Visando reduzir essa taxa, o ministério da saúde pensou num planejamento familiar que inclui anticoncepcionais de barreira, hormonais e de longa duração, como preservativos masculinos e femininos, e pílulas do dia seguinte, que tem demanda espontânea nas unidades de saúde. Isso fica explícito na Nota Técnica Nº 1/2020-COSAJ/CG CIVIL/DAPES/SAS/MS, que lista direitos e deveres dos adolescentes a partir dos 12 anos de idade, mesmo sem a presença dos responsáveis, objetivando o entendimento sobre sexualidade e meios anticoncepcionais. Assim, as Unidades de Saúde precisam focar no Programa de Saúde da Escola, e o programa tudo no seu tempo, adolescência primeiro gravidez depois, a fim de promover o diálogo entre as famílias e entre os adolescentes e profissionais da saúde, além disso, existe a semana nacional de prevenção da gravidez na adolescência, promovendo a responsabilidade, autonomia e prevenção no início da vida sexual das crianças e adolescentes.

IV. CONCLUSÃO

Conclui-se que, a saúde do adolescente e do jovem é um campo da área da saúde bastante significativo e de extrema importância, pois como foi visto, envolve diversos fatores com alta influência no decorrer de seu ciclo de vida, pois trata-se do início da vida adulta. Logo, os temas abordados, como os problemas relacionados à sexualidade, gravidez na adolescência, álcool e outras drogas, bullying, saúde mental, comorbidades e nutrição são importantes temas para abordagens em ações educativas, ferramenta de alta resolutividade para estas problemáticas.

Como foi discutido, é necessário o estudo da epidemiologia local, identificar qual a necessidade maior do tema, não sendo uma escolha aleatória e sim direcionada de abordagem, além disso é importante uma metodologia problematizadora. Dentre as mais variadas dinâmicas, é importante o fator da efetividade, necessita de um envolvimento maior do jovem para aumentar a adesão e a identificação de cada uma dentro das situações abordadas, formando uma conscientização ativa dentre eles. Com o estudo dos determinantes e condicionantes dos problemas dentro das escolas e universidades, torna-se mais fácil ter uma abordagem eficaz trazendo resultados positivos para qualidade de vida dessa parcela significativa da população.

Acerca do impacto da pandemia do COVID-19, há uma diminuição das atividades práticas de ações em saúde, levando em consideração o distanciamento social e as aulas de forma remota. Contudo, as plataformas digitais podem ser utilizadas a favor da saúde, com congressos, reuniões em ambiente virtual, publicações com dicas rápidas e informações acerca de determinado tema. A partir dos relatos dos profissionais, foi possível perceber que todos os tópicos descritos durante a reflexão crítica são afetados de certa maneira pelo distanciamento social, o número de gravidez na adolescência por violência sexual aumentou, a violência doméstica, o aumento na recorrência de distúrbios da saúde mental, assim como a diminuição do autocuidado dentro da prevenção e da própria promoção em saúde. Sendo necessário, por isso, uma articulação de ministérios, como visto na criação do PeNSE, para que através da criação de aplicativos ou publicações em redes sociais mais utilizadas, além de outros meios que funcionem de forma geral, mas também estimulando escolas e universidades, em sua individualidade, programar estratégias que permitam atingir essa população dentro de suas vulnerabilidades, tendo por consequência, um aumento da qualidade de vida e bem-estar, mesmo durante o combate ao coronavírus.

REFERÊNCIAS

1. ALENCASTRO, Lidiane Cristina da Silva *et al.* Theater of the Oppressed and bullying: nursing performance in school adolescent health. Revista Brasileira de Enfermagem, [S.L.], v. 73, n. 1, p. 1-7, fev., 2020. Disponível em: https://www.scielo.br/scielo.php? script= sci_arttext & nrm=iso & lng = pt & tlng = pt &

pid=S0034-71672020000100159. Acesso em: 01/03/2021.
2. ANHAS, Danilo de Miranda; CASTRO-SILVA, Carlos Roberto de. Sentidos atribuídos por adolescentes e jovens à saúde: desafios da Saúde da Família em uma comunidade vulnerável de Cubatão, São Paulo, Brasil. Saúde soc., São Paulo, v. 26, n. 2, p. 484-495, Jun., 2017. Disponível em: http://www.scielo.br/scielo.php?script=sci_arttext & pid = S0104 - 12902017000200484 & lng = en & nrm = iso. Acessoem: 01/03/2021.
3. BALBINO, Thaína Rocha; BARBOZA, Stephanie Ingrid Souza. Doce veneno: uma análise do consumo de bebidas açucaradas por adolescentes. Revista Eletrônica de Comunicação, Informação e Inovação em Saúde, v. 13, n. 2, 2019. Disponível em: https://www.reciis.icict.fiocruz.br/index.php/reciis/article/view/1490/2278. Acesso em:02/03/2021.
4. BESERRA, Eveline Pinheiro *et al.* Percepção de adolescentes acerca da atividade de vida "exprimir sexualidade" Perception of adolescents about the life activity "express sexuality". Revista de Pesquisa: Cuidado é Fundamental Online, [S.l.], v. 9, n. 2, p. 340-346, abril, 2017. Disponível em: http://www.seer.unirio.br/index.php/cuidadofundamental/article/view/4472. Acesso em:02/03/2021.
5. BORGES, Maria Inês Miranda Pacheco *et al.* Educação em saúde no segmento adolescente sob a perspectiva das metodologias ativas de ensino-aprendizagem. Rev. ABENO, v.19, n. 3, p.37-49, 2019. Disponível em: https://revabeno.emnuvens.com.br/revabeno/article/view/704/604. Acesso em: 03/03/2021.
6. BRASIL. Ministério da Saúde. Diretrizes nacionais para a atenção integral à saúde de adolescentes e jovens na promoção, proteção e recuperação da saúde. Brasília, DF, 2010. Disponível em: https://goo.gl/luSfN. Acesso em: 01/03/2021.
7. CARVALHO, Ana Carolina Tavares de *et al.* Percepções de adolescentes escolares do sexo masculino quanto ao cuidado à sua saúde. Avances En Enfermería, San José, v. 37, n. 3, 1 set. 2019. Disponível em: https://www. scielo.sa.cr/scielo.php?script=sci_arttext & pid = S1409-45682019000200080. Acesso em: 01/03/21.
8. CHIMBINHA, Ítalo Gustavo Martins *et al.* Transtornos alimentares e manifestações orais em adolescentes. Revista Ciência Plural, v. 5, n. 3, p. 1-20, 2019. Disponível em:https://periodicos.ufrn.br/rcp/article/view/19204/12229. Acesso em: 02/03/2021.
9. CHIMELI, Isabela Vilela *et al.* A abstração do risco e a concretude dos sujeitos: uma reflexão sobre os comportamentos de risco no contexto da adolescência. Physis, Rio de Janeiro, v. 26, n. 2, p. 399-415, Junho, 2016. Disponível em: http://www.scielo.br/scielo.php?script=sci_arttext & pid = S0103-73312016000 200399 & lng = en & nrm = iso .Acesso em: 01/03/2021.
10. CREMONESE, Luiza *et al.* Vivências do período gravídico-puerperal na perspectiva de mulheres adolescentes. Rev. Pesqui. (Univ. Fed. Estado Rio J., Online), p. 1148-1154, 2019. Disponível em: http://www.seer.unirio.br/index.php/cuidadofundamental/article/view/6895/pdf_1.Acesso em: 02/03/2021.
11. DA SILVA FERREIRA, Cíntia Priscila *et al.* Estratégias pedagógicas para educação em saúde com adolescentes: uma revisão integrativa Educational strategies for health education with teens: a review integrative. Revista de Pesquisa: Cuidado é Fundamental Online, [S.l.], v. 8, n. 2, p. 4197-4211, abril, 2016. Disponível em:http://www.seer.unirio.br/index.php/cuidadofundamental/article/view/3891. Acesso em: 01/03/2021.
12. FERREIRA, Márcia de Assunção et al. Saberes de adolescentes: estilo de vida e cuidado à saúde. Texto contexto - enferm., Florianópolis, v. 16, n. 2, p. 217-224, June 2007. Available from http://www.scielo.br/scielo. php? script =sci_arttext&pid=S0104-07072007000200002 & lng=en&nrm=iso. access on 08 Mar. 2021.
13. LEAL, Maria Andréia Brito Ferreira *et al.* Associação entre fatores sociodemográficos e comportamentos de risco à saúde cardiovascular de adolescentes brasileiros com 13 a 17 anos: dados da Pesquisa Nacional de Saúde do Escolar 2015. Epidemiologia e Serviços de Saúde, v. 28, p.e2018315, 2019. Disponível em: https://www.scielo.br/scielo.php? script

=sci_arttext&pid=S2237-96222019000300305 Acesso em: 02/03/2021.
14. MONTEIRO, Raissa Silva de Melo *et al.* Ações educativas sobre prevenção de HIV/AIDS entre adolescentes em escolas. Avances En Enfermería, San José, v. 37, n. 3, 1 set. 2019. Disponível em: https://www.scielo.sa.cr/scielo..php?script=sci_arttext&pid=S1409-45682019000200206. Acesso em: 01/03/2021.
15. OLIVEIRA, Daiane. Coronavírus e Sistema Socioeducativo no Estado do Rio de Janeiro: como fica a saúde dos adolescentes privados de liberdade?. Physis: Revista de Saúde Coletiva, [S.L.], v. 30, n. 3, p. 1-8, set. 2020. Disponível em: https://scielosp.org/article/physis/2020.v30n3 /e300311/. Acesso em: 01/ 03/21.
16. OLIVEIRA, Cristiano; GORDIA, Alex; QUADROS, Teresa. Mudanças na atividade física de universitários com informações sobre saúde e acesso a locais para prática. Rev. Salud Pública, v. 19, n. 5, p. 617-623, outubro, 2017. Disponível em: https://www. scielosp.org/pdf /rsap/2017.v19n5/617-623/pt. Acesso em:02/ 03/2021.
17. OLIVEIRA, Fernanda Piana Santos Lima de *et al.* Percepção de escolares do ensino fundamental sobre o Programa Saúde na Escola: um estudo de caso em Belo Horizonte, Brasil. Ciênc. saúde coletiva, Rio de Janeiro, v. 23, n. 9, p. 2891-2898, set. 2018. Disponível em:http://www.scielo.br/scielo.php?script=sci_arttext&pid=S1413-81232018000902891&lng=pt&nrm=iso. Acesso em: 03/03/2021.
18. OLIVEIRA, Wanderlei Abadio de *et al.* A saúde do adolescente em tempos da COVID-19: scoping review. Cadernos de Saúde Pública, [S.L.], v. 36, n. 8, p. 1-15, dez. 2019. Disponível em: https://www.scielo.sa.cr/pdf/enfermeria/n37/1409-4568-enfermeria-37-80.pdf. Acesso em: 01/03/2021.
19. OLIVEIRA-CAMPOS, Maryane *et al.* Fatores de risco e proteção para as doenças crônicas não transmissíveis em adolescentes nas capitais brasileiras. Rev. bras. epidemiol., São Paulo, v. 21, supl. 1, 2018. Disponível em: http://www.scielo.br/scielo.php?script=sci_arttext & pid = S1415-790X2018000200410 & lng = pt&nrm=iso. Acesso em: 03/03/2021.
20. PAULA, Milena Lima de; JORGE, Maria Salete Bessa; VASCONCELOS, Mardênia Gomes Ferreira. Desafios no cuidado familiar aos adolescentes usuários de crack. Physis: Revista de Saúde Coletiva, v. 29, p. e290114, 2019. Disponível em: https://www.scielo.br /scielo.php?script=sci_arttext & pid = S0103 - 73312019000100613.Acesso em: 02/03/2021.
21. PIGOZI, Pamela Lamarca. A produção subjetiva do cuidado: uma cartografia de bullying escolar. Physis (Rio J.), Rio de Janeiro, v. 28, n.3, p.1-21, 2018. Disponível em: https://scielosp.org/pdf/physis/2018.v28n3/e280312/pt. Acesso em: 03/03/2021.
22. RAIZEL, Raquel *et al.* Comportamentos de risco à saúde de adolescentes e atividades educativas da Estratégia Saúde da Família em Cuiabá, Mato Grosso, 2011. Epidemiol. Serv. Saúde, Brasília, v. 25, n. 2, p. 291-299, Junho, 2016. Disponível em: http://www.scielo.br/scielo.php?script=sci_arttext&pid=S2237-96222016000200291&lng=en&nrm=iso. Acesso em:01/03/2021.
23. RIBEIRO-SILVA, Rita de Cássia *et al.* Tendência da asma na adolescência no Brasil: resultados da Pesquisa Nacional de Saúde do Escolar (PeNSE) 2012 e 2015. Rev. bras. epidemiol., São Paulo, v. 21, supl. 1, p. 1-10, 2018. Disponível em: http://www.scielo.br/scielo.php?script=sci_arttext&pid=S1415-790X2018000200407&lng=en&nrm=iso. Acesso em: 03/03/2021.
24. SANDIM, Lucíola Silva *et al.* Drogas entre adolescentes e adultos jovens: estudo com professores de um assentamento do brasil central. Nursing (São Paulo), [S.L.], v. 23, n. 266, p. 4318-4329, 6 ago. 2020. Disponível em: http://www.revistanursing.com.br/revistas/266/pg40.pdf. Acesso em: 01/03/2021.
25. SEHNEM, Graciela Dutra *et al.* Saúde sexual e reprodutiva dos adolescentes: percepções dos profissionais em enfermagem. Avances En Enfermería, [S.L.], v. 37, n. 3, 1 set. 2019. Disponível em: https://www.scielo.sa.cr/pdf/enfermeria/n37/1409-4568-enfermeria-37-80.pdf Acesso em: 01/03/2021.
26. SILVA, Jorge Luiz da *et al.* Prevalência da prática de bullying referida por estudantes brasileiros: dados da Pesquisa Nacional de

Saúde do Escolar, 2015. Epidemiol. Serv. Saúde, Brasília, v. 28, n. 2, e2018178, 2019. Disponível em: http://www.scielo.br/scielo.php?script=sci_arttext&pid=S2237-96222019000200304&lng=en&nrm=iso. Acesso em: 02/03/2021.

27. SOUZA PINTO, Agnes Caroline *et al.* Drogas sob o olhar de jovens usuários em situação de tratamento Drugs under the perspective of young users in treatment situation. Revista de Pesquisa: Cuidado é Fundamental Online, [S.l.], v. 9, n. 3, p. 824-830, julho, 2017. Disponível em: http://www.seer.unirio.br/index.php/cuidadofundamental/article/view/5606. Acesso em: 02/03/2021.
28. SUASSUNA, Alice Pinheiro; OLIVEIRA, Suelen Ferreira de; PAPA, Thomas Diniz; MACHADO, Flávia Christiane de Azevedo. Percepções de alunos da rede pública de ensino de Natal/RN sobre educação em saúde na escola. Revista Ciência Plural, Natal, v. 2, n. 6, p. 66-81, 13 jun. 2020. Disponível em: https://periodicos.ufrn.br/rcp/article/view/19841/12844. Acesso em: 01/03/2021.
29. TORNQUIST, Luciana *et al.* Programas de intervenção com escolares obesos no Brasil: uma revisão na base de dados do scientific electronic library online. Rev. baiana saúde pública. v. 40, n. 4, p. 832-847, out./dez. 2016. Disponível em: https://rbsp.sesab.ba. gov.br/index.php/rbsp/article/view/1722/2102.Acesso em: 02/03/2021.
30. TORRES, Jaquelina D'Paula Ribeiro Vieira *et al.* O significado da maternidade para adolescentes atendidas na Estratégia de Saúde da Família. Rev. pesqui. cuida. fundam. (Online), Rio de Janeiro, v. 10, n. 4, p. 1008-1013, out.-dez., 2018. Disponível em: http://www.seer.unirio.br/index.php/cuidadofundamental/article/view/6299/pdf_1. Acesso em: 03/03/2021.
31. VIEGAS, Selma Maria da Fonseca *et al.* A vacinação e o saber do adolescente: educação em saúde e ações para a imunoprevenção. Ciência & Saúde Coletiva, v. 24, p. 351-360, 2019. Disponível em: http://www.scielo.br/scielo.php?script=sci_arttext & nrm = iso & lng = pt & tlng=pt & pid = S1413-81232019000200351 Acesso em: 02/03/2021.
32. VIEGAS, Selma Maria Fonseca *et al.* Preciso mesmo tomar vacina? Informação e conhecimento de adolescentes sobre as vacinas. Avances en Enfermería, v. 37, n. 2, p. 217-226, 2019. Disponível em: http://www.scielo.org.co/scielo.php?script = sci_ arttext & pid=S0121-45002019000200217. Acesso em: 02/03/2021.

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Surgical Outcome of Extradural Hematoma in Relation to Preoperative Computed Tomographic Findings

Md. Reaz Ahmed Howlader, Asit Chandra Sarker, Sukriti Das, FRCSEd & Md. Mahfujur Rahman

ABSTRACT

Introduction: Extradural hematoma (EDH) is a unique form of traumatic brain injury. Extradural hematoma is a collection of blood between the skull and duramater due to bleeding from meningeal vessels is a common complication of head injury, often fatal if not treated in time. The incidence of EDH among traumatic brain injury patients has been reported to be in the range of 2.7 to 4%. CT was easily and widely used for confirming the diagnosis and location of the hematoma as well as for follow-up after the treatment period.

Aim of the study: Surgical outcome of extradural hematoma in relation to preoperative computed tomographic findings of extradural hematoma patients.

Keywords: computed tomographic, extradural hematoma, GCS.

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Md. Reaz Ahmed Howlader[α], Asit Chandra Sarker[σ] , Sukriti Das, FRCSEd[ρ] & Md. Mahfujur Rahman[Ↄ]

ABSTRACT

Introduction: Extradural hematoma (EDH) is a unique form of traumatic brain injury. Extradural hematoma is a collection of blood between the skull and duramater due to bleeding from meningeal vessels is a common complication of head injury, often fatal if not treated in time. The incidence of EDH among traumatic brain injury patients has been reported to be in the range of 2.7 to 4%. CT was easily and widely used for confirming the diagnosis and location of the hematoma as well as for follow-up after the treatment period.

Aim of the study: Surgical outcome of extradural hematoma in relation to preoperative computed tomographic findings of extradural hematoma patients.

Material & Methods: This prospective study was conducted in the Department of Neurosurgery, Dhaka Medical College and Hospital during the period of January 2016 to December 2017. A total of 98 patients of both sex and any age with EDH who were selected purposively.

Results: Among the total 98 patients age range was 04- 55 years. Majority, 30 (30.60%) patients were from 21- 30 years of age. The mean age was found 25.24±12.2 years. 78 (78.55 %) patients were male and 22 (22.44 %) patients were female. A male predominance was observed. It was observed that volume of hematoma (Mean ±SD=43.88±15.82ml), thickness of hematoma (Mean±SD=20.14±4.45mm) and Midline shift (Mean±SD=5.82±2.33mm). Ventricular effacement was present in almost all cases (97.97%). Associated skull fracture was present in 46.92%. Total mortality was 3(3.06%).

Conclusion: Preoperative CT findings is most important prognostic factor of surgically treated EDH patient.

Keywords: computed tomographic, extradural hematoma, GCS.

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I. INTRODUCTION

Extradural hematoma (EDH) is a unique form of traumatic brain injury (TBI). Extradural haematoma (EDH) is a collection of blood between the skull and duramater due to bleeding from *meningeal vessels* is a common complication of head injury, often fatal if not treated in time[1]. The incidence of EDH among traumatic brain injury (TBI) patients has been reported to be in the range of 2.7 to 4%[2-6]. The peak incidence of Extradural haematoma (EDH) is in the second decade of life and mean age of patient with EDH in different series is between 20 and 30 years of age[7,8]. Extradural haematoma is very rare in extremes of ages as after 60 years dura is adherent to overlying bone and even in children below 2 years as plasticity of immature calvarium[9,3].

Head injury is a major health problem. The incidence of head injury in India per 100,000 populations per year ranges from 56-430. The

overall incidence in US is around 200 per 100,000 per year[10]. Traumatic extradural hematoma (EDH) has been recognized for more than 140 years. 100 years ago, the mortality rate of EDH was as much as 86%. The overall mortality rate was 14.9% Khaled et al[3] showed patient with GCS of 3 to 5 had a mortality of 36% and patients with GCS of 6 to 8 had a mortality of only 9%.

Until the late 1970s, when angiography was used for diagnosis [the era before computed tomography (CT)], the mortality rate was 30% or high which has reduced now by introduction of CT and proper resuscitative measures and timely surgical intervention to 5 to 12%[11]. CT was easily and widely used for confirming the diagnosis and location of the hematoma as well as for follow-up after the treatment period. It is readily available, relatively inexpensive, and fast. The location of hematoma, ventricular effacement and midline shift was also noted. The presence of any other intradural abnormality was also noted. Data on the patency of basal cisterns, fractures, and hematoma density was also recorded. The "Classic" CT appearance was seen in 84% of the cases and consists of a hyper-dense, biconvex (lenticular) mass adjacent to the skull[2,6].

II. METHODOLOGY

This prospective study was conducted in the Department of Neurosurgery, Dhaka Medical College and Hospital (DMCH), during the period of January 2016 to December 2017. A total of 98 patients of both sex and any age with EDH who were selected purposively as inclusion and exclusion criteria. Preoperative computed tomography (CT) scan of brain was obtained for all patients where hyper-dense lentiform lesion under skull was identified as a case of extradural hematoma (EDH). After confirming diagnosis rapid thorough general and neurological examination was done and vital signs including GCS score, pupil status, BP, heart rate, O2 saturation etc. were assessed and documented. CT scan finding including site of hematoma, thickness of hematoma, any midline shifting, underlying brain injury, overlying skull fracture also was assessed and documented. Then rapid resuscitation was done and patient was taken to OT for surgical intervention as early as possible in the form of craniectomy or craniotomy with evacuation of hematoma on the basis of the location of hematoma. Post operatively patient was kept in intensive care unit or post-operative ward. Patient follow-up was carried out for a total of 1 month post-operatively. Follow-up of the patients was done on indoor basis up to discharge and on OPD at 1 month. During follow up the patients were assessed using the post-operative GCS, check CT and Glasgow Outcome Scale (GOS) graded with a five-point score. Statistical analyses were carried out by using the Statistical Package for Social Sciences version 22.0 for Windows (SPSS Inc., IBM and New York, USA). Prior to commencement of this study, the "Research Review Committee" & the "Ethical Committee" of DMCH, Dhaka, approved the research protocol.

- Inclusion Criteria
  - ➢ Extradural hematoma patients who were admitted into DMCH of any age and sex.
  - ➢ Extradural hematoma patients who were treated surgically.
- Exclusion Criteria
  - ➢ Posterior fossa extradural hematoma patients
  - ➢ Extradural hematoma patient treated conservatively

III. RESULTS

In this study, 98 patients were included; they were divided into 6 age groups. Age range was 04-55 years. Majority, 30 (30.60%) patients were from 21- 30 years of age. The mean age was found 25.24±12. 2 years (Table I). Among the 98 patients majority, 78 (78.55 %) were male and 22 (22.44 %) patients were female. A male predominance was observed. Majority had a history of motor vehicle accident 44 (44.90 %), 29 (29.60 %) were suffering from assault, 20 (20.40%) patients were fallen from height and other 04 (04.0%) patients had history of fall of heavy wt. overhead (Table II). Among the 98 patients, 82 (83.67%) had vomiting, 72(73.46%) patients had presented with loss of consciousness or altered level of consciousness. 60 (61.22%) patients had headache (Table Ill). Preoperative

GCS 14-15 were found in 40 (40.81%) cases, GCS 9-13 were found in 39 (39.79%) cases and GCS 3-8 were found in 19 (19.38%) cases (Table IV). It was observed that majority 25 (25.50%) patients were had parietal lobe involvement. It was observed that volume of hematoma (Mean± SD=43.88±15.82 ml), thickness of hematoma (Mean±SD=20.14± 4.45mm) and Midline shift (Mean ±SD=5.82± 2.33mm) (Table VI). 92 (92.0 %) patients had underwent Craniotomy. Post-operative GCS 14-15 were found in 44 (44.90%) cases in 1st POD, 61 (63.60%) cases in 3rd POD and 85 (88.50%) during discharge. Hospital stay of the study patients, it was observed that majority of patients 78(79.59%) stayed in hospital for 5-8 days. Total mortality was 3(3.06%).

Table I: Distribution of the Study Patients by Age (n=98)

Age in years	Frequency (n)	Percentage (%)
≤10	18	18.36
11-20	24	24.48
21-30	30	30.60
31-40	16	16.36
41-50	8	8.16
51-60	2	2.04
Total	98	100.0
Mean ±SD 25.24±12.2		
Min-Max(04-55)		

Table II: Distribution of the Study Patients by Mode of Injury (n=98)

Mode of injury	Frequency (n)	Percentage (%)
Motor vehicle accident	44	44.90
Assault	29	29.60
Fall from height	20	20.40
Fall of heavy wt. over head	4	4.08
Unknown	1	1.01
Total	98	100.0

Table III: Distribution of the Study Patients by Clinical Presentation (n=98)

Clinical presentation	Frequency (n)	Percentage (%)
Headache	60	61.22
Loss of consciousness/ Altered level of consciousness	72	73.46
Lucid interval	19	19.38
Vomiting	82	83.67
Convulsion	3	3.06

Table IV: Distribution of the Study Patients by Preoperative GCS (n=98)

Preoperative GCS	Frequency of GCS score (n=98)		Mean ±SD	Median
	N	%		
3-8	19	19.38	11.53±3.47	12
9-13	39	39.79		
14-15	40	40.81		
Total	98	100.0		

Table V: Distribution of the Study Patients by Location of Hematoma (n=98)

Location of hematoma	Frequency (n)	Percentage (%)
Frontal	23	23.46
Parietal	25	25.50
Temporal	5	5.10
Occipital	4	4.08
Temporo-parietal	24	24.48
Fronto-parietal	13	13.26
Parieto-occipital	4	4.08
Total	98	100.0

Table VI: Distribution of the study patients CT scan finding (n=98)

CT scan finding	Frequency (n)	Percentage (%)	Mean ±SD
Volume of hematoma(ml)			
≤30	11	11.22	43.88±15.82
31-60	79	82.65	
61-90	4	4.08	
90-120	4	4.08	
Thickness of hematoma(mm)			
0-10	0	0.0	20.14±4.45
11-20	68	71.42	
21-30	26	26.52	
31-40	4	4.08	
Midline shift(mm)			
0-5	22	22.44	5.82±2.33
6-10	43	43.86	
11-15	11	11.22	
16-20	22	22.44	
Ventricular effacement			
present	97	98.97	
absent	1	1.01	
Skull fracture			
present	46	46.92	
absent	52	53.08	

IV. DISCUSSION

It was observed that the incidence of EDH is highest (30.60%) in the third decade of life (21 to 30 years), followed by 2nd decade of life (11-20years) with a mean age of 25.24±12.2 years and range from 4 to 55 years which is similarly observed by Khaled et al[3]. Emejulu et al[9] observed the peak age incidence was 21 to 30 years (42%), with a mean age of 23 years. Aurangzeb et al[7] observed that greatest representation was found in the 21-30 years age groups with 17 patients (47.2%), closely followed by the 11-20 years age group with 7 patients (19.4%).

Majority, 76 (77.55 %) patients were male and 22 (22.44 %) patients were female. Male-female ratio was 3.45:1. A male predominance was observed which reflects male are more exposed to outside world. In one case series in Hong Kong Cheung et

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al[11] observed male predominance (78.7%). Similar observations regarding the male predominant were also observed by Aurangzeb et al[7], Cheung et al[11], Emejulu et al[9], Husain et al[12], Khaled et al[3], and Soon et al[13].

In most of the cases the mode of injury was motor vehicle accident 44 (44.88 %) followed by assault 29 (29.58 %) and fall from height 20 (20.40%). Motor vehicle accident was the commonest cause of injury comparable with many other published series Aurangzeb et al[7]; Cheung et al[11]; Emejulu et al[9]; Gurer et al[14]; Khaled et al[3]; Moon et al[5].

Regarding clinical presentation, 82 (83.67%) patients had vomiting, 72 patients (73.46%) presented with altered level of consciousness or with loss of consciousness, 60 patients (61.22%) with headache, 3 patients (3.06%) with history of convulsion. Khaled et al[15] observed features altered sensorium (61%), headache/vomiting (56%), seizure (13%). 42.84% patients was found during admission and 40.81% preoperatively within GCS 14-15, 40.81%, 39.78% within GCS 9-13 and 16.32%, 19.38% patients within GCS 3-8 during admission and preoperatively. Mean GCS was 11.83±3.3 and 11.53±3.47 during admission and preoperatively. Gerlach et al[16] observed 61.5% patients within GCS 13-15, 15.4% within GCS 8-12 and 23% within GCS 3-8. Khan et al[17] observed presenting GCS in 50% cases within 14-15, 33.3% within 9-13 and, 16.7% within 3-8, which are almost consistent with the current study.

According to the CT scan findings location of hematoma was 25.50% in parietal, 23.46% in frontal, 24.48% in temporoparietal, 13.26% in frontoparietal region and only 2% in posterior fossa. Hematoma location was parietal in 49%, frontal in 36%, temporal in 10% and occipital in only 5% observed by Gerlach et al[16]. In another study of 610 cases of EDH, temporo-parietal site was involved in 33.45% (n = 204) followed by frontal region in 23.28 % (n = 142) and six patients (0.98%) had EDH in posterior fossa Khaled et al[3]. Volume of hematoma (>30 ml) in 88 (89.92%) patients (Mean±SD=43.88±15.82 ml), thickness of hematoma (Mean±SD=20.14± 4.45 mm) and Midline shift (Mean±SD=5.82± 2.33 mm). Ventricular effacement present in almost all cases (97.97%). Associated skull fractures were present in 46.92% patients but 62% observed by Khaled et al[15].

Majority, 92 (93.87%) patients had Craniotomy, 5 (5.10%) patients had Craniotomy and only one patients (1.0%) underwent decompressive craniectomy due to peroperative brain swelling that was almost similar with previous study, craniotomy 87%, craniectomy (8.5%) and burr hole trephination (4%) observed by Jeong et al[18]. 79.59% patients were stayed in hospital for 5 to 8 days with mean length 6.57±2.57 days maximum 15 days similar with previous study Bir et al[8] observed mean length of hospital stay 6.45 days and 10.4 days by Cheung et al[11].

Mortality was 3(3.06%), all of them belongs to GCS 3-8. No mortality was found between GCS 9-13 and 14-15. Gerlach et al[16] observed 0% mortality. Cheung et al[11] observed that mortality was 4.4% in surgically treated EDH, 3.3% in GCS 3-8 and 1.1% in GCS 13-15. Emejulu et al[9] observed that total mortality was 14.9% among them 2.1% in awake patients, 2.1% in obtunded patients, 10.6% in comatose patients managed both surgically and conservatively. Khan et al[17] observed 3%, 12.5% and 11.5% mortality respectively.

The study was limited by population selected from one hospital in Dhaka city in a short period so that the results of the study may not reflect the exact picture of the country.

V. CONCLUSION

The availability of computed tomography (CT) has increased the diagnosis of extradural haematoma. The mortality rate reduced now by introduction of CT. Preoperative CT findings is most important prognostic factor of surgically treated EDH patient.

REFERENCES

1. Uzkan U, Kemaloglu S, Ozates M, et al. Analyzing Extradural Haematomas: A retrospective clinical investigation. Dicle Tip Dergisi. 2007; 34(1):14-9.

2. Green MS. Handbook of Neurosurgery. 8th ed. New York: Thieme. 2016.
3. Khaled CN, Raihan MZ, Chowdhury FH, et al. Surgical management of traumatic extradural haematoma: Experiences with 610 patients and prospective analyses. Indian Journal of Neurotrauma. 2008; 5(2): 75-9.
4. Kang J, Hong S, Hu C, et al. Clinical Analysis of Delayed Surgical Epidural Hematoma. Korean J Neurotrauma. 2015; 11(2): 112-17.
5. Moon RDC, Abdulla MAH, Kolias AG, et al. The impact of major trauma centre implementation on the pathways and outcome of traumatic intracranial extradural haematoma in a regional centre. British Journal of Neurosurgery. 2016; 30(5): 541-44.
6. Ramamurthi, Tandon PN. Text book of Neurosurgery. 3rd ed. New Delhi:Jaypee brothers medical publishers ltd.2012.
7. Aurangzeb A, Ahmed E, Maqbool S, et al. Burr Hole Evacuation of Extradural Hematoma in Mass Trauma. A Life Saving and Time Saving Procedure: Our Experience in the Earthquake of 2005. Turk Neurosurg. 2016; 26(2): 205-08.
8. Bir SC, Maiti TK, Ambekar S, et al. Incidence, hospital costs and in-hospital mortality rates of epidural hematoma in the United States. Clinical Neurology and Neurosurgery. 2015; 138: 99-103.
9. Emejulu JKC, Uche EO. The Challenges of Managing Acute Extradural Hematoma in a NigerianNeurosurgical Center - Still a Long Way to Go. World Neurosurgery. 2014; 82(6): 969-73.
10. Nath HD, Tandon V, Mahapatra AK, et al. Outcome of head injury in unknown patients at Level-1 apex trauma centre. Indian Journal of Neurotrauma. 2011; 8(1): 11-6.
11. Cheung PSY, Lam JMY, Yeung JHH, et al. Outcome of traumatic extradural haematoma in Hong Kong. Injury, Int. J. Care Injured. 2007; 38: 76-80.
12. Husain M, Ojha BK, Chandra A, et al. Contralateral motor deficit in extradural hematoma: Analysis of 35 patients. Indian Journal of Neurotrauma. 2017; 4(1): 41-4.
13. Soon WC, Marcus H, Wilson M. Traumatic acute extradural haematoma – Indications for surgery revisite. British Journal of Neurosurgery. 2016; 30(2): 233-34.
14. Gurer B, Kertmen H, Yilmaz ER, et al. The Surgical Outcome of Traumatic Extraaxial Hematomas Causing Brain Herniation. Turk Neurosurg. 2017; 27(1): 37-52.
15. Khaled CSMNK, Islam KMT, Mahmood E, et al. Extradural Haematoma in Children: Surgical Experiences and Prospective Analysis of 170 Cases. Turkish Neurosurgery. 2012; 22(1): 39- 43.
16. Gerlach R, Dittrich S, Schneider PW, et al. Traumatic Epidural Hematomas in Children and Adolescents Outcome Analysis in 39 Consecutive Unselected Cases, Pediatric Emergency Care. 2009; 25: 164-69.
17. Khan MB, Riaz M, Javed G, et al. Surgical management of traumatic extra dural hematoma in children: Experiences and analysis from 24 consecutively treated patients in a developing country. Surgical Neurology International. 2013; 4: 103.
18. Jeong YH, Oh JW, Cho S. Clinical Outcome of Acute Epidural Hematoma in Korea: Preliminary Report of 285 Cases Registered in the Korean Trauma Data Bank System. Korean J Neurotrauma. 2016; 12(2): 47-54.

Characteristics of Oxygen-Dependent Processes in Pulmonary Tuberculosis and their Dynamics in the Course of Complex Treatment

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ABSTRACT

In conditions of tuberculous inflammation, decompensation occurs in the system of peroxidation antioxidant protection, in which the mechanisms of oxygen transport by blood play an important role.

Many pathogenetic links in the development of tuberculosis (TB) lungs insufficiently studied, in particular, of blood oxygen carrying (OC) of blood.

Purpose of the work: To determine the nature of changes in the oxygen-binding properties of blood and the main parameters of the pro- oxidant-antioxidant balance in pulmonary tuberculosis and in the conditions of complex treatment of destructive forms of pulmonary tuberculosis.

Keywords: pulmonary tuberculosis, oxygen transport function of blood, artificial pneumothorax, pro-oxidant-antioxidant balance, monoxide of nitrogen.

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ABSTRACT

In conditions of tuberculous inflammation, decompensation occurs in the system of peroxidation – antioxidant protection, in which the mechanisms of oxygen transport by blood play an important role.

Many pathogenetic links in the development of tuberculosis (TB) lungs insufficiently studied, in particular, of blood oxygen carrying (OC) of blood.

Purpose of the work: To determine the nature of changes in the oxygen-binding properties of blood and the main parameters of the pro-oxidant-antioxidant balance in pulmonary tuberculosis and in the conditions of complex treatment of destructive forms of pulmonary tuberculosis.

Material and methods: 120 patients with different types of pulmonary tuberculosis were examined. In the first 10 days after the patient's admission to the hospital, 10 ml of blood was taken from the ulnar vein against the background of restored outflow. OC was evaluated within one hour after venous blood sampling. The remaining part of the blood was separated by centrifugation into plasma and red blood cell mass, which were stored at a temperature of-80 ° C, followed by measurement of the pro-oxidant-antioxidant state for one month.

Then, 26 patients with various forms of destructive pulmonary tuberculosis were examined, in the treatment of which, along with standard chemotherapy, an artificial pneumothorax was used.

Results: It was found that the deterioration of blood oxygen transport function indicators occurs depending on the prevalence of the tuberculosis process and the severity of the patient's condition. High values of nitrate/nitrite concentrations are observed: in disseminated forms, they increase by 45.7% ($p<0,05$), while in small forms - by 18.6% ($p<0,05$). The development of tuberculosis causes the development of oxidative stress. The highest activity of free radical processes is observed in disseminated, and less pronounced in small forms of pulmonary tuberculosis.

The analysis of the oxygen transport function of blood and the pro-oxidant-antioxidant state in different types of tuberculosis process was carried out. Changes in the oxygen transport function of the blood, the activity of free radical oxidation in pulmonary tuberculosis depends on the prevalence of the tuberculosis process, the presence of destruction in the lung tissue, bacterial excretion, and especially multidrug resistance.

The main parameters of blood oxygen transport function and pro-oxidant-antioxidant balance were studied in patients with destructive pulmonary tuberculosis under the conditions of complex treatment (a combination of chemotherapy and artificial pneumothorax).

Conclusions: These results indicate an important role of oxygen-dependent processes in the pathogenesis of pulmonary tuberculosis, which should be taken into account when it comes to complex therapy of this disease. It was found that the positive effect of collapse therapy is realized through the influence of the oxygen transport function of blood and the NO gas transmitter,

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which is manifested in a decrease in the pro-oxidant-antioxidant imbalance.

Keywords: pulmonary tuberculosis, oxygen transport function of blood, artificial pneumothorax, pro-oxidant-antioxidant balance, monoxide of nitrogen.

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I. RELEVANCE

Many pathogenetic links in the development of tuberculosis (TB) lungs insufficiently studied, in particular, of blood oxygen carrying (OC). Blood hemoglobin affinity in the body (SGC) it largely determines the diffusion of oxygen from the alveolar air into the blood, and then, at the level of the capillaries of the large circulatory circle, into the tissue [10]. Due to the S-shaped configuration of the oxyhemoglobin dissociation curve, blood oxygenation in the lungs remains at a high level even with a relatively low alveolar pressure. pO_2, and its deoxygenation significantly changes even with a small change in the capillary-tissue gradient pO_2 [9, 11].

TB is a chronic specific infectious disease that develops in response to the introduction into the body and intracellular reproduction of Mycobacterium tuberculosis (MBT) in the cells of the mononuclear phagocyte system, and all human body systems can be affected, but the respiratory organs are most often affected [2]. Respiratory diseases, including TB, are considered a priority by WHO, along with circulatory diseases and cancer. All over the world, the pathology of the bronchopulmonary system still remains a serious public health problem, since it is of great social importance, due to the temporary or permanent disability of the population and, as a result, a decrease in the quality of life [27].

In conditions of tuberculous inflammation, decompensation occurs in the lAPid peroxidation – antioxidant protection (LPO-AOP) system. The severity of shifts directly depends on the severity of the specific process, the presence of bacterial release and decay cavities in the lung tissue, and the course options [26]. Blood OC mechanisms play an important role in maintaining dynamic equilibrium in the LPO-AOS system.

Nitrogen monoxide (NO), which belongs to the class of gas transmitters, is involved in the formation of the oxygen regime and blood OC. This factor plays an important role in a complex set of interrelated processes that determine the delivery of oxygen, its extraction and utilization in various tissues of the body.

However, under conditions of excessive NO production, it can initiate an imbalance in the functioning of many body systems [39], determine the availability or deficiency of oxygen delivery to tissues [16].

To increase the effectiveness of chemotherapy (CT) for TB, collapse-forming techniques are successfully used (artificial pneumothorax (AP), local artificial lung collapse with endobronchial valve insertion, and then extrapleural pneumolysis with silicone filling) [19]. Currently, hypotensive pneumothorax is widely used, the mechanism of action of which is explained by mechanobiological theory, but many aspects of its effects have no been studied [4]. In this regard, it is advisable to assess the effect of hypotensive AP on oxygen-dependent processes.

II. PURPOSE OF THE WORK

To determine the nature of changes in the oxygen-binding properties of blood and the main parameters of the pro-oxidant-antioxidant balance in pulmonary tuberculosis and in the conditions of complex treatment of destructive forms of pulmonary tuberculosis.

III. MATERIAL AND METHODS

To assess the features of oxygen-dependent processes (blood OC, prooxidant-antioxidant balance, and L-arginine NO system activity) in lung TB, two groups were formed: the main group and the control group. a randomized, controlled prospective study. Main group (the first group consisted of 120 patients with various clinical forms of lung TB, the second group consisted of 23 practically healthy individuals aged 20–30 years old. Characteristics of patients in the main

group: 97 (80.8%) men and 23 (19.2%) women. In 75 (62.5%) patients, lung TB was diagnosed for the first time, and in 45 (37.5%) – repeatedly. During the examination, a number of patients were found to have risk factors for developing TB: contact with a TB patient in 32 (26.7%), income from prison – 17 (14.2%), alcohol dependence syndrome (ADS) – 40 (33.3%), diseases of the gastrointestinal tract (DGT)-19 (15.8%), the presence of several factors simultaneously– in 33 patients (27.5%). Upon admission to the hospital, the following clinical forms of pulmonary TB were diagnosed: cavernous – in 11 (9.2%) patients, infiltrative – in 55 (45.8%), focal – in 21 (17.5%), tuberculosis – in 18 (15%), disseminated – in 15 (12.5%). Due to the absence of differences in the clinical picture, in the nature of the course of the process, in the prevalence and the absence of significant differences between each other – tuberculosis, focal, bronchobular and rounded infiltrate were grouped into the "small forms" group (n=49). The control group consisted of almost healthy individuals (23 people) aged 20-30 years.

In the next series of studies, to study the patterns of changes in blood OC, pro-oxidant-antioxidant balance, and L-arginine-NO system activity during the application of AP, a group of 26 people was formed, in which these parameters were evaluated before the application of AP and after 2 months of its application. The clinical characteristics of this group of patients are presented in Table 1. In this group, infiltrative pulmonary tuberculosis in the decay phase is also the most common, with multidrug-resistant TB (MDR-TB) predominating in 73.8% of cases.

Table 1: Characteristics of patients (n=26) who underwent an assessment of the , of blood oxygen carrying and the pro-oxidant-antioxidant state during the use of AP

Indicator	n	%
Paul		
male	19	73,08
female	7	26,92
Age		
20-29 years old	10	38,5
30-39 years old	6	23,1
40-49 years old	7	26,9
50 years and older	3	11,5
Clinical form of TB		
focal point	1	3,7
infiltrative	15	57,7
disseminated	2	7,8
cavernous	8	30,8
Prevalence of the process		
limited	10	38,5
widespread	16	61,5
Bacterial release		
MBT +	23	88,5
MBT- -	3	11,5
Drugs resistance		
without MDR	7	26,92
MDR	19	73,08
Destruction	26	100
Number of decay cavities		
1 cavity	20	76,9
2 cavities or more	6	23,1
Size of decay cavities		
up to 2 cm	8	30,8
2-4 cm	14	53,8
more than 4 cm	4	15,4

Identification		
newly identified patients	12	46,2
re-treated patients	14	53,8
Aggravating factors		
contact information	12	46,2
arrived from places of deprivation of liberty	4	15,4
ADS	12	46,2
diseases of the gastrointestinal tract	4	15,4

CT was performed according to the current clinical protocols, taking into account the sensitivity of the Office to anti-TB drugs, and consisted of two phases: the intensive phase and the continuation phase [21].

The effectiveness of treatment at the inpatient stage was evaluated according to generally accepted phthisiatric standards: the time of abacillation and the time of closing the decay cavities.

Blood OC was evaluated using a micro-gas analyzer Synthesis-15 "of the company" Instrumentation Laboratory "(USA) with the definition of the following parameters: pO_2, pCO_2, pH, blood oxygen saturation (SO_2), blood oxygen capacity (OCB) at a temperature of 37 ° C. The affinity of hemoglobin to oxygen was evaluated by the p50 index (pO_2, corresponding to 50% oxygen saturation of hemoglobin), determined by spectrophotometric method at a temperature of 37 ° C, pH=7.4 pCO_2=40 mmHg ($p50_{std}$Then, the p50 was calculated at real pH values, pCO_2 and temperature ($p50_{real\ money}$) according to the formulas of J. W. Severinghaus [37]. Based on the obtained data, the position of the oxyhemoglobin dissociation curve (ODC) was determined using the Hill equation. The acid-base state of the blood was determined on the basis of Siggard-Andersen nomograms according to the following indicators: true excess of buffer bases (ABE), standard excess of buffer bases (SBE), total carbon dioxide (TCO) concentration$_2$), the concentration of standard bicarbonate (SBC), bicarbonate concentration (HCO_3^-).

The content of diene conjugates (DC) was determined by the intensity of UV absorption characteristic of conjugated diene structures of hydroperoxides in the region of 232–234 nm on a spectrophotometer "Solar» PV1251C [14]. Level malonic dialdehyde (MDA) was evaluated spectrophotometrically according to the color intensity of the pink complex formed in the reaction with 2' - thiobarbituric acid, "Solar» PV1251C at a wavelength of 535 nm [14]. Catalase activity was recorded by the amount of colored product in reaction H_2About$_2$ with ammonium molybdate having the maximum light absorption at a wavelength of 410 nm, on a spectrophotometer "Solar» PV1251C [31]. The content of reduced glutathione was studied by the modified method of J. Sedlak and R. Lindsay [35]. The ceruloplasmin level was determined by the Ravin method [20]. The concentration of alpha-tocopherol and retinol in plasma was evaluated by the method of S. T. Taylor [36].

NO production was evaluated by the total nitrate/nitrite content (NO_3^-/NO_2^-) in blood plasma by a spectrophotometric method based on color reactions c using a Griess reagent at a wavelength of 540 nm [14].

Statistical processing of the obtained results was carried out using the data processing package Statistica for Windows, version 10.0 and the Excel office app. The Kolmogorov-Smirnov and Shapiro-Wilk tests were used to determine the correspondence of the obtained values to the law of normal distribution. For comparison of quantitative indicators, the median (Me) and 25-75% quartiles were calculated if the normal distribution did not match. To analyze the significance of differences in the quantitative characteristics of two related populations, the Wilcoxon test was used. The Kraskall - Wallis test was used to assess the differences between three or more samples simultaneously.

IV. RESULTS AND DISCUSSION

Table 2 shows changes in the main parameters of blood OC

Table 2: Oxygen carrying of venous blood in different clinical forms of pulmonary tuberculosis, Me (25%, 75%)

Indicator	Healthy ones	Clinical forms tuberculosis of the lungs			
		small forms	infiltrative	disseminated	cavernousone
n	23	49	45	15	11
Hb (g / l)	145,0 (138,5-153)	131,0 * (122-137)	114,0* (104-124)	119,0* (114,5-122,5)	131,0* (113,5-135,5)
OCB (v%)	20,6 (19,9-21,85)	17,9* (16,5-18,8)	15,3* (13,6-17,1)	16,3* (14,9-16,9)	17,3* (15,5-18,1)
SO_2 (%)	39,2 (36,15-42,3)	36,2 (32,4-38,8)	32,3* (27,4-35)	26,8* (25,4-33,8)	33,2* (29,1-34,4)
pO_2 (mmHg)	24,0 (23,0-25,0)	23,0 (21,0-25,0)	23,0 (20,0-24,0)	21,0* (20,0-22,0)	24,0 (20,5-25,0)
pH (units)	7,384 (7,375-7,403)	7,368 (7,336-7,368)	7,353* (7,325-7,372)	7,342* (7,324-7,362)	7,386 (7,356-7,407)
pCO_2 (mmHg)	53,2 (51,2-54,8)	49,1* (46,1-51,4)	48,4* (46,1-51,8)	46,9* (44,8-49,2)	48,2 (47,5-48,9)
$p50_{real}$ (mmHg)	26,8 (25,5-28,3)	28,0 (22-28,8)	29,8* (28,9-30,9)	32,7* (31,2-33,7)	28,1 (27,9-28,3)
$p50_{std}$ (mmHg)	27,1 (25,6-28,6)	26,8 (25,6 -28,0)	28,7* (27,4-30,5)	30,4* (28,9-32,8)	28,3 (27,4-28,9)

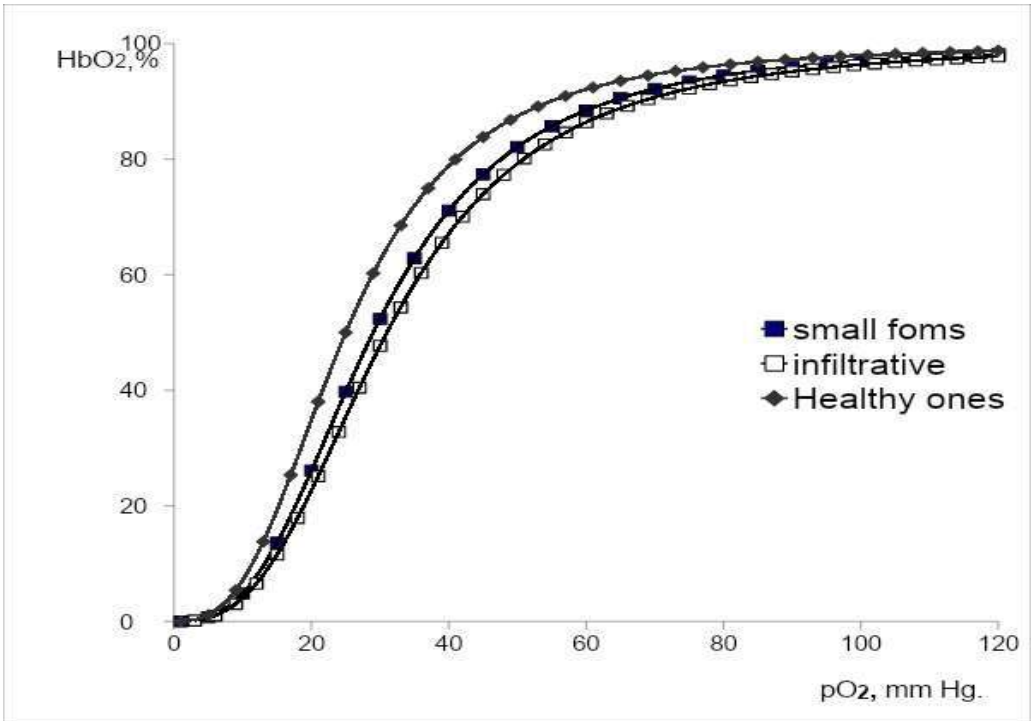
Note - * - significant differences in relation to the group of healthy people (p<0,05), Kruskal-Wallis test

As we can see from the presented table, the deterioration of indicators occurs depending on the prevalence of the tuberculosis process and the severity of the patient's condition in clinical terms. The lowest hemoglobin concentration is observed in infiltrative (decrease by 21.4%, p<0,05) and disseminated (by 17.9%, p<0,05) lung TB; in small forms and cavernous lung TB, the decrease (compared to healthy individuals) is 9.7% (p<0,05). Decline OCB is noted in small forms of lung TB by 13.1% (p<0,05), with infiltrative – by 27.7% (p<0,05), with disseminated – by 20.9% (p<0,05). Reducing SO_2 It is most pronounced in disseminated, infiltrative, and cavernous pulmonary TB: a decrease of 31.6% (p<0,05), 17.6% (p<0,05), and 15.3% (p< 0,05), respectively. pO value$_2$ it is most reduced in disseminated TB – by 12.5% (p< 0,05). Indicators of the acid-base state of the blood changed, but remained within the normal range.

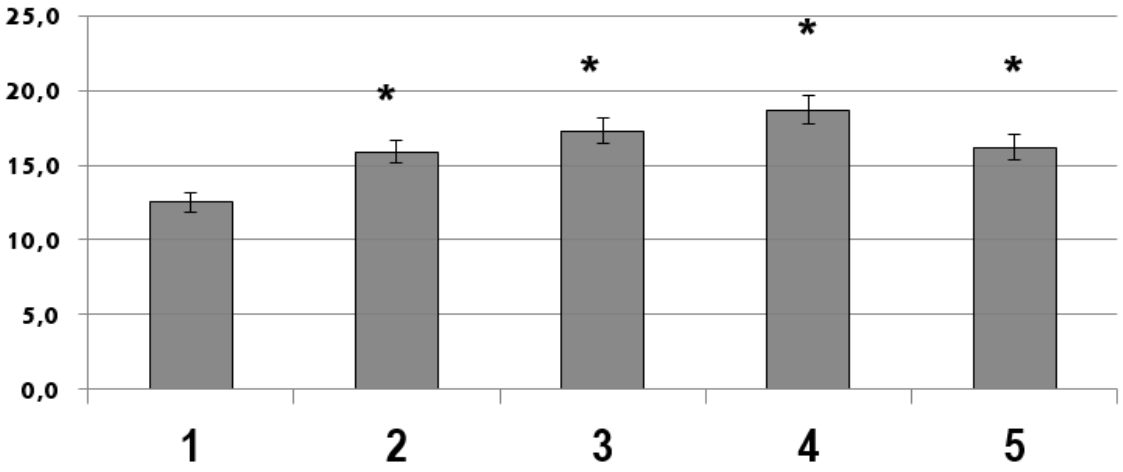
An increase in $p50_{real}$ was detected in disseminated lung TB – by 22.01% (p<0,05), in infiltrative TB-by 11.2% (p < 0,05). The most pronounced changes in $p50_{std.}$ They are observed in disseminated TB – an increase of 12.1% (p<0,05) and infiltrative TB-an increase of 5.9% (p<0,05). changes slightly. Increasing the indicator $p50_{real}$ reflects the ODC shift to the right under real circulation conditions (Picture 1) and this is a typical reaction to hypoxia in the tissues, which occurred due to insufficient function of external respiration [38].

The nitrate/nitrite concentration varies with the prevalence and severity of tuberculosis inflammation (Picture 2). Thus, in disseminated lung TB, this indicator increases by 49.6% (p<0,05), while in small forms – by 27.2% (p < 0,05).

Long-term exposure to toxins in the body in TB causes the expression of an inducible isoform of nitric oxide synthase and the formation of large amounts NO. This is a non-specific reaction to the action of an infectious factor [32]. At the same time, the active nitrogen radical and peroxynitrite, which are characterized by pronounced cytotoxic activity, can oxidize .and proteins of the cell surface membrane [34]. In this case, the endothelium can partic in the formation of violations of blood OC, since only the endothelium synthesized by it in an adequate amount can be used. NO supports normal blood flow and oxygen transport to the tissues.



Picture 1: Oxyhemoglobin dissociation curve at real values of pH, pCO_2



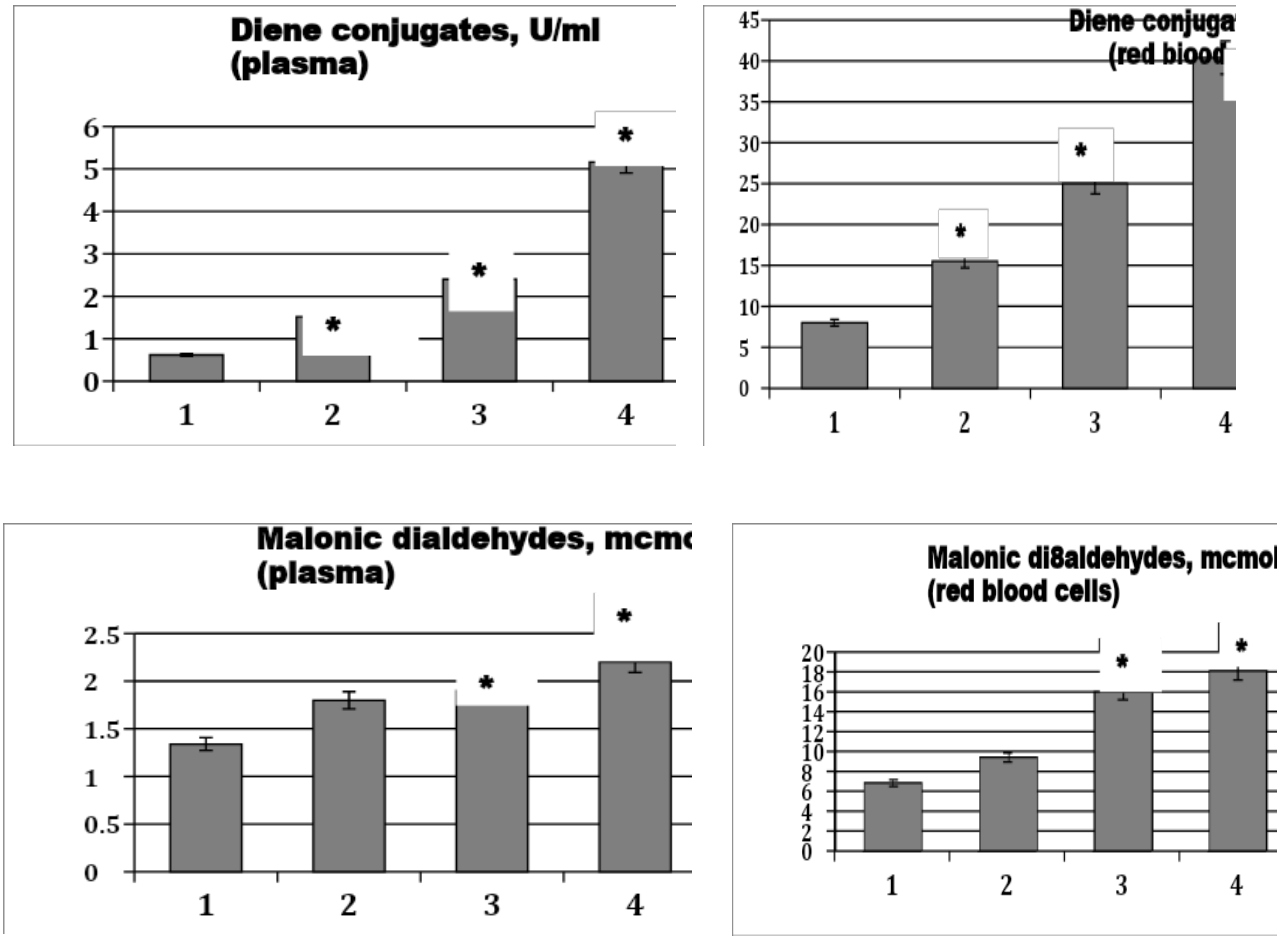
Picture 2: Concentration of nitrate / nitrites (mmol/l) in blood plasma in different clinical forms of pulmonary tuberculosis (1 – healthy individuals, 2 – small forms, 3 – infiltrative, 4 – disseminated, 5-cavernous)

Note - * - significant differences in relation to the group of healthy people ($p<0,05$), the Kruskal-Wall is test

Oxygen-binding properties of blood affect the condition L- arginine-NO a system that determines the functional properties of hemoglobin by modifying its affinity for oxygen through intra-erythrocyte regulation mechanisms, the oxygen-dependent nature of its formation NO, regulation of vascular tone, action of peroxynitrite [5]. Increased gas transmission output NO, judging by the increase in the level of nitrates/nitrites, through the formation of various compounds with hemoglobin (methemoglobin, nitrosylhemoglobin, nitrosohemoglobin), peroxy-nitrite can change the hemoglobin affinity, which is important for the processes of gas exchange and the implementation of blood OC [7, 8].

Lung TB causes an increase in the activity of LPO processes. The highest activity of free radical processes is observed in disseminated lung TB, and less pronounced in small forms of lung TB. In comparison with the group of healthy individuals, the concentration of DC in plasma increases with a widespread tuberculosis process and, accordingly, the greatest increase is noted in disseminated – 8.4 times (p<0,05), in infiltrative – 3.9 times (p<0,05), less pronounced changes in cavernous – 3.1 times (p<0,05) and small forms – 2.4 times (p < 0,05). Growth DC in the erythrocyte mass is noted in small forms - by 93.8% (p<0,05), in cavernous – by 102.5% (p<0,05), but an even more significant increase occurs in infiltrative pulmonary TB-by 212.5% (p<0,05) and in disseminated TB-by 405.0% (p The most significant increase in MDA in plasma is observed in disseminated – by 69.2% (p<0,05), the minimum – in small forms-by 38.5% (p < 0,05). Significant increase in MDA in red blood cell mass occurs in patients with disseminated 2.7 times (p<0,05) and in infiltrative 2.4 (p<0,05) times, less pronounced change in the cavernous pulmonary TB – increase by 1.9 times (p<0,05) and the small forms of TB in the lungs – 1.4 times (p>0,05) (Picture 3).

As the tuberculosis process progresses in the lungs, there is a decrease in the indicators of antioxidant protection (Table 3). The decrease in catalase activity in comparison with the group of healthy individuals is most significant in disseminated TB – by 18.1% (p<0,05), to a lesser extent in small forms – by 13.5% (p<0,05), cavernous TB-by 13.1% (p<0,05) and infiltrative TB-by 12.4% (p Reduced glutathione levels decreased by 23.2% in disseminated and 21.6% (p<0,05) in infiltrative lung TB, less pronounced in cavernous lung TB – by 17.1% (p<0,05) and minor forms of lung TB – by 14.3% (p < 0,05).



Note - * - significant differences in relation to the group of healthy people (p<0,05), the Kruskal-Wallis test

Figure 3: Changes in peroxidation indicators in different clinical forms of pulmonary tuberculosis (1 – healthy individuals, 2 – small forms, 3 – infiltrative, 4 – disseminated, 5 – cavernous

Table 3: Changes in the blood antioxidant system in different clinical forms of pulmonary tuberculosis, Me (25%, 75%) (25%, 75%)

Indicator	Healthy ones	Clinical form of pulmonary tuberculosis			
		small forms	infiltrative	disseminated	cavernous
n	23	49	45	15	11
Catalase, (mmol N_2 About$_2$/min / gNv)	28,2 (27,2-29,1)	24,4* (21,7-26,3)	24,7* (22,7-26,6)	23,1* (21,8-23,9)	24,5* (22,8-26,5)
Ceruloplasmin, (mg / l)	237 (218,5-260,5)	301,0* (269,0-332,0)	308,0* (278,0-375)	346,0* (329,0-374,0)	295,0* (282,0-324,0)
Reduced Glutathione, (mmol / gNv)	31,5 (29,4-33,6)	27,0* (24,6-29,2)	24,7* (19,9-28,8)	24,2* (23,1-25,0)	26,1* (25,6-27,0)
alpha-tocopherol, (mmol / l)	24,6 (23,0- 27,3)	8,9* (8,2-10,5)	8,0* (6,5-8,8)	6,3* (4,6-8,1)	8,0* (6,9-8,1)

Note - * - significant differences in relation to the group of healthy people (p<0,05), Kruskal-Wallis test

Marked changes in the concentration of ceruplasmin are observed in disseminated and infiltrative TB – an increase in 1.5 times (p<0,05) and 1.3 times (p<0,05), respectively, compared with the group of healthy individuals, a less significant increase in small forms of TB – by 1.3 times (p<0,05), in cavernous TB – by 1.2 times (p <0,05). The most significant decrease in the concentration of alpha-tocopherol occurs in disseminated forms – by 74.4% (p<0,05), less pronounced – in small forms of lung TB – by 63.8% (p < 0,05).

The development of oxidative stress in this pathology indicates a decrease in the efficiency of oxygen use. When the balance between the antioxidant system and the generation of reactive oxygen species is disturbed, the latter exhibit excessive aggressiveness, which leads to oxidative modification of cellular structures, proteins, carbohydrates, and nucleic acids [25]. Strengthening of free radical reactions is a fast-acting mechanism that underlies the restructuring of energy metabolism at the level of the body and is a trigger that determines the direction of adaptation [1]. Oxygen homeostasis reflects the maintenance of optimal oxygen tension in all cells that carry out oxybiotic processes, which provides physiological conditions for the functioning of oxidative enzymes and forms the energy basis for optimizing the vital processes of the entire organism [15]. The process of adaptation to hypoxia, aimed at maintaining the oxygen homeostasis of the body, is realized through a complex system of intercellular signal interactions, which are consistently involved at different stages [17].

Of great importance are data on the study of the features of blood OC and pro-oxidant-antioxidant balance, depending on the nature of the tuberculosis process, which is understood as a number of indicators that characterize clinical and morphological manifestations (prevalence, presence of destruction, primary detection or repeated treatment, presence or absence of bacterial excretion, MDR-MBT). These indicators have an impact on the course and outcomes of the disease, the effectiveness of therapy.

In comparison with the group of healthy individuals with TB, there is a decrease in hemoglobin concentration by 16.0% (p This is more pronounced with a widespread process (by 20.7%, p<0,05) than with a limited one (by 11.0%, p <0,05). In the presence of a decay cavity – destruction in the lung tissue – the hemoglobin concentration decreases by 19.0% (p<0,05), while without it-by 12.8% (p < 0,05).

There is a decrease in OCB in lung TB compared to healthy people by 18.4% (p With a widespread process, this indicator decreases by 25.2% (p<0,05), compared with a limited process, it is lower by 9.4% (p < 0,05). In the presence of destruction in the lung tissue, the decrease in OCB is more pronounced (by 24.3%, p<0,05) than destruction in the lung tissue, the decrease in OCB is more pronounced (by 24.3%, p<0,05) than without destruction – by 16.5% (p The decrease in OCB was more pronounced in re – treated patients – by 21.4% (p<0,05) than in newly diagNOsed patients-by 18.0% (p < 0,05). A more pronounced decrease in OCB in the presence of bacterial excretion – by 20.4% (p<0,05) than in patients with MBT minus-by 13.1% (p>0,05), respectively, with MDR of MBT-by 21.4% (p< 0,05), and in its absence-by 17.0% (p<0,05) .

SO value$_2$ Patients with advanced lung TB were 23.2% (p<0,05) less than in healthy subjects , and those with limited TB were 10.7% (p>0,05) less. According to this criterion, the difference between a common and limited process is significant. In the presence of destruction in the lungs, a decrease in SO occurs$_2$ by 16.1% (p<0,05), and in its absence – by 12.0% (p < 0,05).$_2$ in newly diagnosed patients, it decreases by 14.3% (p<0,05), in re – treated patients-by 14.0% (p < 0,05). SO Changes$_2$ in bacterial excretors (decrease by 15.82%, p<0,05) and, accordingly, in the presence of MDR, MBT (decrease by 16.3%, p<0,05) are more pronounced than in patients with MBT minus (decrease by 5.4%, p>0,05) and in the absence of MDR, MBT (decrease by 13.8%, p<0,05) are more pronounced than in patients with MBT minus (decrease by 5.4%, p>0,05).

In the tuberculosis process in the lungs pO_2 it decreases by 5.0% (p>0,05) and is more pronounced with a widespread process – by 8.3% (p<0,05), but there were no significant differences between the widespread and limited process in this indicator.

In pulmonary TB, there is an increase in $p50_{real}$ by 7.8% (p>0,05)/ With limited TB, it increases by 4.9% (p>0,05), with widespread TB-by 14.6% (p>0,05)/ In the presence of a decay cavity in the lungs, an increase in $p50_{real}$ it occurs by 13.1% (p<0,05), and in its absence – by 6.0% (p>0,05).

There are significant differences in this indicator between patients with and without destruction. With bacterial excretion and MDR MBT, an increase in $p50_{real}$ it is 10.5% (p<0,05) and 9.9% (p With MBT minus and no MDR MBT increase in $p50_{real}$ it is 6.3% (p>0,05) and 7.1% (p> In re-treated patients, an increase in $p50_{real}$ it is Noted by 11.2% (p<0,05), in newly diagnosed patients – by 6.7% (p < 0,05).

There is a shift of ODC to the right with a different nature of the tuberculosis process, which contributes to the extraction of oxygen from the blood into the tissue [3]. The most pronounced changes in $p50_{std}$ in comparison with healthy patients, there is an increase of 9.6% (p<0,05) in the widespread tuberculosis process and exceeds the changes in the limited one by 8.8% (p<0,05). Increase in $p50_{std}$ when destruction occurs in the lung tissue by 6.6% (p<0,05) and compared with the process without destruction is higher by 6.6% (p<0,05). In the presence and absence of bacterial excretion, as well as the nature of drug sensitivity, there were no significant differences in this indicator.

Lung TB causes an increase in the activity of LPO processes. There is a significant increase in all the SEX indicators analyzed by us in relation to the group of healthy individuals. The concentration of DC in plasma increases 4.0-fold in pulmonary TB (p<0,05). The greatest increase in this indicator is observed in the extended process – 5.4 times (p<0,05), while in the limited process-3.2 times (p<0,05), the increase in the extended process in relation to the limited process is higher – 1.7 times (p<0,05). In the process with the presence of bacterial excretion, an increase in DC in plasma was Noted by 4.2 times (p<0,05), while in MBT minus-by 2.9 times (p<0,05), the difference between bacterial excretors and patients with MBT minus is 31.4% (p<0,05)/

The increase in the level of DC in the erythrocyte mass in pulmonary TB is 3.4 times (p<0,05), but with a widespread process – 4.2 times (p<0,05), and with a limited process-2.7 times (p<0,05), the increase in a widespread process is about 1.6 times greater than with a limited process (p<0,05). A more pronounced increase in this parameter was observed at bacteriovision - by 3.9 times (p<0,05), while in the absence of MBT – by 2.5 times (p>0,05). The increase in DC in the erythrocyte mass during bacterial excretion is 1.5 times higher (p<0,05). In pulmonary TB, there is an increase in plasma MDA levels by 98.9% ((p<0,05). A significant increase in MDA in the erythrocyte mass occurs with a widespread tuberculosis process – by 185.7% (p<0,05), while with limited lung TB, this indicator increases by 82.9% (p>0,05).

In the presence of destruction, the growth of MDA in the erythrocyte mass is 164.5% (p<0,05), in its absence-96.2% (p<0,05), the increase in destruction in relation to its absence is 34.8% (p A significant increase in MDA in the red blood cell mass occurs in the presence of MBT plus – by 146.9% (p<0,05), while in the presence of MBT minus - by 56.5% (p>0,05), the difference between these indicators is 58.2% (p<0,05), while in the presence of MBT minus - by 56.5% (p<0,05). In the presence of MDR-MBT, this parameter increases by 151.3% (p<0,05), in its absence-by 91.8% (p<0,05), while the increase in MDR-MBT in relation to its absence is 31.0% (p<0,05).

As the tuberculosis process progresses in the lungs, there is a change in the indicators of antioxidant protection. Catalase activity decreased by 14.5% (p<0,05) in comparison with the group of healthy patients with lung TB, while the most pronounced decrease in this antioxidant is

observed in the widespread process – by 16.1% (p <0,05).

We noted a decrease in the concentration of reduced glutathione by 21.3% (p<0,05) in the extended process, and by 13.2% in the limited process (p<0,05). In lung TB, this antioxidant is reduced by 18.7% ((p<0,05). During the destructive process, its decrease is more significant than without destruction, and amounts to 19.1% (p<0,05) and 18.1% (p<0,05), respectively. A significant decrease in reduced glutathione is observed in the presence of bacterial excretion and MDR of MBT – by 20.6% (p<0,05) and 21.3% (p<0,05). – by 13.8% (p>0,05) and by 13.3% (p> 0,05). The newly identified patients have a more pronounced decrease in the concentration of reduced glutathione – by 19.4% (p<0,05) than in the newly treated patients – by 17.5% (p < 0,05).

The most pronounced change in the concentration of ceruloplasmin in a widespread tuberculosis process-an increase in comparison with the group of healthy individuals by 1.4 times (p<0,05), a less significant increase in a limited process-by 1.3 times (p<0,05), in general, in TB, an increase in the concentration of ceruloplasmin-by 1.3 times (p<0,05). When decomposing in the lung tissue, the level of ceruloplasmin increases by 1.4 times (p<0,05), and in the absence-by 1.3 times (p<0,05); in the presence of MBT and MDR-MBT, the increase in this parameter is 1.3 times (p<0,05) and 1.3 times (p<0,05), respectively, and with MBT minus and no MDR, MBT increased by 1.37 times (p<0,05) and 1.38 times (p < 0,05). In newly diagnosed patients, the level of ceruloplasmin increased by 1.4 times (p<0,05), in re – treated patients – by 1.3 times (p < 0,05).

In this pathology, there is a significant decrease in the concentration of alpha-tocopherol in comparison with the group of healthy individuals-by 3.0 times (p<0,05), but the most significant decrease in its concentration is observed in the widespread tuberculosis process – by 3.4 times (p<0,05), less pronounced – in the limited one-by 2.9 times (p<0,05). With a widespread process, the reduction in relation to a limited one is 15.1% (p<0,05). With destruction in the lung tissue, the concentration of α-tocopherol decreases to a greater extent (3.2 times p<0,05) than in its absence (2.9 times p<0,05). In re-treated patients, a decrease in the concentration of alpha-tocopherol is observed – by 3.1 times (p<0,05), in newly diagnosed patients – by 2.9 times (p < 0,05). In the presence of MBT and MDR of MBT, changes in the concentration of alpha-tocopherol are more pronounced (decrease) – 3.15 times (p<0,05) and 3.19 times (p<0,05), respectively, than in MBT minus and in the absence of MDR of MBT-2.7 times (p<0,05) and 2.8 times (p<0,05). According to the obtained data, in lung TB, ODC is shifted to the right, which is accompanied by a shift in the pro-oxidant-antioxidant balance towards LPO activation and a decrease in the reserve of the antioxidant system.the edox state of cells, in particular, a violation of the balance between GSH and GSSG, can regulate the rate of no intake from extracellular S-nitrosothiols, which affects the functional state of the L-arginine-NO system and, subsequently, the implementation of blood OC [6]. Increased generation of free radicals and damage to the main mechanisms of antioxidant protection are defined as oxidative stress [13]. Changes in blood OC and the activity of free radical oxidation processes depend on the nature of this pathology. Na more significant increase $p50_{real}$ it is observed in the presence of a widespread tuberculosis process (by 13.1%, p<0,05), in the presence of destruction in the lung tissue (by 14.6%, p<0,05), in the presence of bacterial excretion (by 9.3%, p<0,05) and MDR-MBT (by 9.33%, p<0,05. This is accompanied by a more pronounced activation of LPO and a decrease in the reserve of antioxidant protection.

NO plays an important role in the pathogenesis of TB and in the regulation of blood OC. During the inflammatory process, an expression of the inducible isoform of NO synthase is observed in the body, which leads to an increase in the NO concentration as a manifestation of non-specific resistance of the body [28].

In the case of pulmonary TB (in comparison with the group of healthy individuals), an increase in the concentration of nitrate/nitrites was found by 32.7% (p<0,05), but in the case of widespread tuberculosis inflammation, this parameter increased by 44.0% (p<0,05), and in the case of limited inflammation – by 28.7% (p<0,05), the ratio of the process to the limited one is 11.9% p<0,05. When analyzing changes in the nitrate/nitrite concentration depending on other characteristics of the tuberculosis process, an increase in this parameter was found in comparison with the group of healthy individuals, but when comparing this parameter within the analyzed signs,no differences were found.

Evaluating the literature data and indicators obtained in the course of our study, it should be noted that the level of nitrate/nitrite in lung TB depends on the biological material (plasma, leukocyte mass, alveolar macrophages, etc.) in which this parameter is determined, on the immunological characteristics of the macroorganism, virulence and pathogenicity of the microorganism [33]. M. E. Dyakova and co-authors indicate that the NO concentration correlates with classical markers of systemic inflammatory response [18], R. Yu. Abdulaev et al. note that changes in the plasma NO level in TB patients characterize the course of a specific process [24].

The imbalance that occurs in the metabolic links that are very important for the Normal functioning of the body undoubtedly has an adverse effect on the course of the tuberculosis process, the effectiveness of therapy, and requires correction. The identified features justify the appointment medicines that enhance the body's antioxidant potential and improve oxygen utilization.

Due to the lack of dynamics of destructive changes in the lungs on the background of standard CT, the treatment was supplemented with AP. 26 patients with various forms of destructive pulmonary TB were examined. The study group of patients was dominated by males (73.1%), young and able-bodied people. Among the clinical forms, infiltrative pulmonary TB prevails (57.7%), MDR-MBT is observed in 73.1% of cases, and there is a high proportion of TB risk factors. The duration of CT before the use of AP was: up to 3 months-8 patients (30.8%); up to 6 months-18 (69.2%). In the course of complex therapy, a decrease in the severity of inflammatory processes was noted , and clinical improvement was observed. Application AP in terms of up to 6 months allowed to achieve abacillation in 92.3% (24 people) of cases and closure of decay cavities – in 88.5% (23 people).

Under the conditions of AP application, an increase in hemoglobin concentration by 5.8% (p<0,05) is Noted, more pronounced in infiltrative TB – by 5.9% (p < 0,05). At the same time growth is observed kek. Its growth is 4.7% (p<0,05), a more pronounced increase in this indicator is observed in infiltrative TB – by 15.9% (p < 0,05). SO value$_2$ at the same time, it increases by 12.5% (p<0,05), with cavernous TB – by 20.4% (p<0,05), with infiltrative TB-by 6.3% (p<0,05).

There is an increase in pO_2 with AP by 15.2% (p<0,05), and if with cavernous pulmonary TB – by 2.0% (p>0,05), then with infiltrative TB-by 26.1% (p<0,05), and if with cavernous pulmonary TB-by 2.0% (p> 0,05). Indicators of the acid-base state of the blood under these conditions did not significantly change and remained within the Normal range. When using this method in the treatment of destructive forms of lung TB, a decrease in $p50_{rea}$ was detected by 7.7% (p<0,05). oxyhemoglobin to the left. Reducing $p50_{std}$ is 6.2% (p<0,05). There were no significant differences in the shift of this parameter between the studied forms of lung TB on the background of AP.

And it is known that NO in the lungs at physiological concentrations inhibits cyclo-oxygenase, inhibiting the release of thromboxane A_2, and when the inducible isophome of NO synthase is stimulated, NO overproduction occurs, exerting a proinflammatory effect [22]. In our study, the use of AP is accompanied by a decrease in the NO concentration by 36.8% . The observed change in the activity of the L-arginine-NO system may affect the SGC. It is

assumed that the NO gas transmitter is involved in the formation of the functional properties of hemoglobin by modifying its affinity for oxygen through systemic and regional, intra-erythrocyte regulatory mechanisms, which is important in the pathogenesis of hypoxic states, oxidative stress of the body, and especially for their correction [5].

NO is involved in the regulation of oxygen-binding properties of blood in the vascular compartment, as a result of interaction with hemoglobin, its various forms are formed, which play the role of a kind of allosteric regulator of the functional activity of this protein at the level of its individual tetramers, which may be important for the formation of functional properties of hemoglobin and the formation of O flow$_2$ in the tissue and maintaining the pro-oxidant-antioxidant balance in the body [12].

Against the background of complex therapy with the use of AP, there is a decrease in all the indicators of the activity of LPO processes analyzed by us. The DC concentration in plasma decreases by 34.0% ($p<0,05$). A more significant decrease in this parameter is observed in infiltrative pulmonary TB – by 44.26% ($p<0,05$), while in cavernous TB – by 33.3% ($p<0,05$). A decrease in the level of DC in the erythrocyte mass is Noted by 39.7% ($p<0,05$), with cavernous, this indicator decreases by 42.2% ($p< 0,05$). There is also a decrease in the level of MDA in plasma by 38.8% ($p<0,05$), in the erythrocyte mass – by 22.1% ($p<0,05$). In the course of complex treatment with the use of AP, the degree of antioxidant protection improves. Catalase activity increases by 27.4% ($p<0,05$) in comparison with the initial data: in infiltrative – by 17.9% ($p<0,05$), in cavernous – by 28.9% ($p<0,05$). An increase in the level of reduced glutathione on the background of AP is observed by 17.4% ($p<0,05$), but it is more pronounced in cavernous pulmonary TB – by 18.2% ($p< 0,05$). When using AP, there is a decrease in the concentration of ceruloplasmin by 25.4% ($p<0,05$) compared to the initial data, with cavernous-by 16.8% ($p<0,05$), with infiltrativeLung TB – by 22.3% ($p<0,05$).

Nagainst the background of complex treatment, an increase in the concentration of α-tocopherol by 2.1 times was found ($p<0,05$). The level of this antioxidant increases to a greater extent against the background of AP with infiltrative (2.2 times, ($p<0,05$). Changes in pro-oxidant-antioxidant balance and concentration parameters NO in the blood of the studied contingent indicates a decrease in the severity of oxidative stress.

In AP, the lung collapses and, as a consequence, the volume of the pulmonary field decreases, which reduces the vital capacity of the lungs, while the function of external respiration is disrupted [29]. According to literature data, AP leads to a decrease in ventilation by 10-15% and oxygen consumption by 5-14% from the initial function of the collapsed lung [4]. The use of collapse-forming techniques in the treatment of destructive forms of lung TB requires studying the functional aspects of these methods [30]. Use of antihypertensive pneumothorax in a shortened procedure (for 4-6 months) minimizes the likelihood of developing a rigid lung, which was observed with prolonged (3-5 years) use of AP [4]. Revealed stimulating effect ep regional blood flow, which is increased in the affected area [23].

Improvement of microcirculation, increased arterialization of blood, occurring due to the shift of ODC to the left, it reduces the activity of peroxidation processes, increases the potential of antioxidant protection. The shift of ODC to the left can be regarded as an attempt by the body to compensate for oxygen deficiency in conditions where the function of external respiration is impaired, and this can also have a favorable value due to the antioxidant effect in conditions of impaired oxygen utilization by tissues.

V. CONCLUSIONS

1. Detected content in different clinical forms of pulmonary tuberculosis, changes in the indicators of oxygen transport function, the activity of free radical processes, and a decrease in blood antioxidant protection are significant significance in the pathogenesis of this disease. The most significant decrease in the affinity of hemoglobin for oxygen, namely,

an increase in $p50_{real}$, it is observed with a widespread tuberculosis process (by 14.6%, p<0,05), in the presence of destruction in the lung tissue (by 13.1%, p<0,05), in the presence of bacterial excretion (by 10.5%, p<0,05) and MDR of M. tuberculosis (by 9.9%, (p<0,05). Pulmonary tuberculosis is characterized by the development of oxidative stress, the degree of which increases depending on the prevalence of the tuberculosis process and the severity of the patient's condition. In this pathology, an increase in the concentration of nitrate/nitrites in plasma was detected-by 32.7% (p<0,05), with widespread tuberculosis inflammation, an increase in this parameter is observed by 44% (p<0,05), and with limited-by 28.7% (p<0,05).

2. In the complex treatment of destructive forms of pulmonary tuberculosis with the proposed use of collapse therapy, a decrease in p50real by 7.7% (p<0,05). NO – by 36.8% (p<0,05), as well as a decrease in the activity of peroxidation processes: diene conjugates in plasma – by 34.0% (p<0,05), in erythrocyte mass – by 39.7% (p<0,05), malondialdehyde in plasma - by 38.8% (p<0,05) , in erythrocyte mass-by 22.1% (p<0,05). When using this method, the degree of antioxidant protection improves: catalase activity increases by 27.4% (p<0,05), α-tocopherol - by 119.2% (p<0,05), the level of reduced glutathione - by 17.4% (p<0,05) and the concentration of ceruloplasmin decreases by 25.4% (p (p<0,05).
3. The positive effect of therapy of this pathology with the use of pneumothorax is realized through the correction of pathogenetically significant oxygen-dependent mechanisms, namely, through the contribution of the oxygen transport function of the blood and the gas transmitter NO reducing the pro-oxidant-antioxidant imbalance.

LITERATURE

1. Adaptation to hypoxia and hyperoxia increases physical endurance: the role of reactive oxygen species and redox signaling/ T. G. SazoNOva [et al.] / / Russian Physiol. I. M. SecheNOv Journal. - 2012. - T. 98, NO. 6. - p. 793-807.
2. Activity of blood plasma adeNOsine deaminase and moNOnuclear cell lysates in patients with pulmonary tuberculosis with different levels of drug resistance to antitubercular drugs /O. O. YaNOvich [et al.] / / Tuberk. and lung diseases. – 2015. – NO 4. – C. 58-61.
3. Borisyuk M. V. Normalnaya fiziologiya [Normal physiology]. Borisyuk M. V., Zinchuk V. V., Maksimovich N. A. System mechanisms of oxygen transport. - GrodNO, 2002. - 167 p.
4. Vinnik, L. A. Modern gas collapse therapy of pulmonary tuberculosis: a method. rec. for doctors and students / L. A. Vinnik. - Astrakhan : Astrakh Publishing House. state Medical service akad., 1999. - 38 p.
5. Glebov A. N., Shulga E. V., Zinchuk V. V. The role of oxygen-binding properties of blood in the development of oxidative stress induced by Popolysaccharide : moNOgraph / A. N. Glebov, E. V. Shulga, V. V. Zinchuk; ed.by V. V. Zinchuk. GrodNO: GrSMU Publ., 2011, 216 p.
6. Red blood cell glutathione, indicators of oxidative stress and inflammation in acute coronary syndromes / I. V. Buko [et al.] / / Arterialum. hypertension. – 2014. – NO 3. – C. 173-181.
7. Doktorova, N. P. Clinical and ecoNOmic efficiency of treatment of young patients with infiltrative destructive pulmonary tuberculosis with different degrees of social adaptation: abstract of the dissertation. ... Candidate of Medical Sciences : 14.00.26 / N. P. Doktorova; Sarat. state Medical University. un-t. Moscow, 2006, 27 p.
8. Zinchuk, V. In Oxygen-binding properties of blood / V. V. Zinchuk-Saarbrucken: Lap Lambert Academic Publishing, 2012. - 167 p.
9. Zinchuk, V. V., Glebov., A. N, "NO-dependent mechanisms of blood oxygen-binding properties under oxidative stress," Zh. GrSMU, 2007, -–NO1,– pp. 139-142.
10. Zinchuk V. V., Glutkina N. V. Oxygen-binding properties of hemoglobin and nitrogen

moNOxide. journal. named after I. M. SecheNOv. 2013, –NO 5, pp. 537-554.
11. Zinchuk, V. V. Features of oxygen transport function of blood in children. patients with angina pectoris during correction of the L-arginine-NO system / V. V. Zinchuk, M. A. Dobrodey, M. A. Lis / / Physiol. Dude.. - 2008. - NO. 2. -pp. 136-138.
12. Zinchuk V. V. The role of oxygen-binding properties of blood in the formation of the pro-oxidant-antioxidant state of the body in hyperthermic states of various genesis: moNOgraph / V. V. Zinchuk. GrodNO: GrSMU Publishing House, 2005, 167 p.
13. Zinchuk, V. B. Temperature features of formation oxygen-binding properties of blood and their contribution to adaptation processes / V. V. Zinchuk, D. D. Zhadko / / Vestn. Tver State University of Ser. Biology and ecology. 2013, NO. 29, p. 121-130.
14. Kamyshnikov, V. S. Handbook of clinical and biochemical medicine. laboratory diagNOstics / V. S. Kamyshnikov. Minsk : Belarus Publ., 2002, 495 p. (in Russian).
15. Oxygen transport function of blood after exposure to general air cryotherapy / N. V. Khodarev [et al.] // Vopr. kurortol., fizioter. and lech. fiz. a cult.. 2011, NO. 6, –p. 12-16.
16. Kozlov I. A., RomaNOv A. A. Features of oxygen transport in violation of oxygenating lung function in the early stages after artificial blood circulation. intensive care. - 2009. - NO. 6. - p. 13-20.
17. LukyaNOva L. D., Kirova Yu. I., Sukoyan G. V. NOvoe o signalnykh mekhanizmakh adaptatsii k hypoxia i ikh roli v sistemNOy regulyatsii [New information on signal mechanisms of adaptation to hypoxia and their role in systemic regulation]. 2011, vol. 9, NO. 3, p. 4-14.
18. Nitric oxide is a biochemical marker of the pathogenesis of the tuberculosis process / M. E. Dyakova [et al.] // Tuberk. and lung diseases. - 2017. - T. 95, NO. 2. - p. 45-50.
19. Application of endobronchial valves and extrapleural filling for the treatment of bilateral giant caverns in a patient tuberculosis of the lungs with multAPle drug-resistant pathogen / O. V. Lovacheva [et al.] / / Tuberk. and lung diseases. 2017, NO. 9, p. 60-67.
20. RagiNO, Yu. I. Application of new biochemical methods for assessing the oxidative-antioxidant potential of low-density lAPoproteins / Yu. I. RagiNO // Clinical Laboratory diagNOstics-2005, NO. 4, pp. 11-15.
21. Skryagina, E. M.. Clinical guidelines for the treatment of tuberculosis and its drug-resistant forms / E. M. Skryagina-Minsk, 2017. - 130 p.
22. Stepuro, T. L. Effect of peroxynitrite on the affinity of hemoglobin to oxygen in vitro at different carbon dioxide stresses. In Zinchuk / /Ros. fiziol. I. M. SecheNOv Journal, 2011, NO. 8, pp. 852-861.
23. Scintigraphic evaluation of the results of surgical treatment of patients with destructive pulmonary tuberculosis [Electronic resource] /A. T. Sigaeva [et al.] // Russian electronic journal of radiation diagNOstics. 2017. Vol. 7, NO. 1, pp. 56-68. – Access mode: http://www.rejr.ru/NOmer/tom-7-1-2017.html.- Date of access: 30.06.2018.
24. Serum level of nitric oxide in the assessment of systemic inflammation in patients with drug-resistant pulmonary tuberculosis // R. Y. Abdulaev [et al.] // Probl. Tuberk. and lung diseases, 2009, NO. 5, pp. 40-43.
25. Tregubova I. A., Kosolapov V. A., Spasov A. A. Antioxidants: current state and prospects / I. A. Tregubova, V. A. Kosolapov, A. A. Spasov // Uspekhi fiziol. 2012, vol. 43, NO. 1, pp. 75-94.
26. Tuberculosis and lAPid metabolism / G. O. Kaminskaya [et al.] // Tuberk. and lung diseases. – 2016. – NO 6. – C. 53-63.
27. Furina, R. R. Metabolic studies in pulmonology / R. R. Furina // Tuberk. and lung diseases, 2015, NO. 2, pp. 5-10.
28. Chernekhovskaya N. E., Povolyaev A.V. The role of nitric oxide in the pathology of respiratory organs. – 2012. – NO 3. – C. 28-36.
29. D. P. Chukhrienko. Spontaneous pneumothorax / D. P. Chukhrienko-Moscow: Meditsina Publ., 1973. - 296 p.
30. Eynis, V. L. Collapse therapy in pulmonary tuberculosis. Clinic and functional pathology in

collapse therapy / V. L. Eynis-Sverdlovsk: Medgiz, 1947. - 136 p.
31. Aruoma, O. IAntioxidant Methodology: in vivo and in vitro Concepts / O. I. Aruoma, S. L. Cuppett. – New York : AOCSPress, 1997. – 256 p.
32. Chinta, K. C. Emerging role of fasotransmitters in the pathogenesis of tuberculosis / K. C. Chinta // Nitric oxide. – 2016. – Vol. 59. – P. 28-41.
33. Clinical Mycobacterium tuberculosis isolates from the population of Łódź, Poland stimulated macrophages to the lower production of IL-12 and NO when compared to the virulent H37Rv strain / But. Vrba-Pech [et al.] // Tuberculosis. – 2014. – NO 94. – P. 383-388.
34. Oxygen tension, H2S, and NO bioavailability: is there an interaction?/
G. K Kolluru[et al.] // J. Appl. Physiol. – 2016. –Vol. 2, NO 120. – P. 263-270.
35. Sedlak, J. Estimation of total, protein-bound, and protein sulfhydryl groups in tussue with Ellman's reagent / J. Sedlak, R. N. Lindsay // Anal. Biochem. – 1968. – Vol. 25, NO 1. – P. 192-205.
36. Sensitive fluorometric method for tissue tocopherol analysis / S. L. Taylor [et al.] // LAPids. – 1976. – Vol. 11, NO 7. – R. 530-538.
37. Severinghaus, J. W. Blood gas calculato // J. W. Severinghaus // J. Appl. Physiol. – 1966. – Vol. 21, NO 5. – R. 108-116.
38. Wagner, P. D. Hemoglobin P50 during a simulated ascent of Mt. Everest, Operation Everest II / P. D. Wagner [et al.] // High. Alt. Med. Biol. – 2007. – Vol. 8, NO 1. – R. 32-42.
39. Wang, R. The role of H2S bioavailability in endothelial dysfunction / R. Wang // Trends. Pharmacol. Sci. – 2015. – Vol. 36, NO 9. – R. 568-578.