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CLINICOPATHOLOGICAL ANALYSIS AND ASSOCIATION OF FINE NEEDLE ASPIRATION WITH THE DIFFERENT LYMPH NODE LESIONS IN RURAL SINDH.

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ABSTRACT

BACKGROUND: Using Fine needle aspiration cytology FNAC as a mode of investigation is helpful in knowing the common patterns of lymphadenopathies which assist in diagnosing the clinical pathology where there is a dilemma in reaching the final diagnosis. FNAC is effectively used for both superficial and deep soft tissue masses and the most commonly targeted sites are the lymph nodes, breast, thyroid, salivary glands, and skin thus eliminating the need for unnecessary surgical interventions such as open biopsies. **OBJECTIVE:** The aim of this study was to observe the most common diagnosis for FNAC in patients presenting with lymph node swellings in the outpatient department in patients of both genders and all age groups. **METHODOLOGY:** In this cross-sectional study, 297 patients were recruited from the rural areas of Sindh. All the samples were collected from "The Laboratory" from "February 2019" to "December 2019" after taking informed consent. The sampling method in this study was non-probability consecutive sampling. FNAC was performed in each patient after observing all aseptic measures, slides were prepared and evaluated by a panel of histopathologists. Quantitative data was represented by Mean and Standard Deviation while the qualitative data was represented by frequency and percentages. The chi-square test was used to determine the association of different clinical variables with the diagnosis. **RESULTS:** 297 patients, 113 (38%) were males and (184) 62% were females. The subjects' ages ranged from 1 -75 years and were divided into 3 respective groups, (0-19 years, 20-39 years, and ≥40 years). The majority of the patients (128, 43.1%) fell in the 0-19 age group, followed by 124 (41.8%) patients in the 20-39 age group and only 45 individuals (15.2) were ≥40 years of age. The most common site of lymph node involvement was observed to be the cervical group with a total of 227 cases, of which 135 (45.5%) affected the right cervical group and 92 (31%) affected the left cervical group. This was followed by the right axillary group with 12 cases (4%) and the sub-mental group with 10 cases (3.4%). A sum of 192 cases was diagnosed with granulomatous inflammation by the histological findings, out of which 161 (54.2%) cases were Tuberculous/Chronic Specific Lymphadenitis and the remaining 31 (10.4%) were of tuberculous abscess. The next common lesion observed was Chronic non-specific lymphadenitis with 87 cases (29.3%). 12 cases (4%) were Suspicious of Malignancy. A significant association was observed between the cause of lymphadenopathy and the age of the patient (p value= 0.002), the site of the lymph node (0.002). **CONCLUSION:** In the current survey female of younger age groups were more frequently presented with right cervical lymphadenophies having chronic non-specific lymphadenitis. Age and site of the lymph node involved had an association with the diagnosis of FNAC.

KEYWORD: syphilis, prevalence, HBV, HCV, blood, donors

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INTRODUCTION

Fine needle aspiration cytology (FNAC) is a minimally invasive procedure that is extensively used in outpatient settings[1] It is cost-effective, easy to perform, and fairly accurate making it suitable for use in developing countries, especially for diagnosing lymphadenopathies.[1, 2] Using FNAC as a mode of investigation is helpful in knowing the common patterns of lymphadenopathies which assist in diagnosing the clinical pathology where there is a dilemma in reaching the final diagnosis.[3] FNAC is effectively used for both superficial and deep soft tissue masses and the most commonly targeted sites are the lymph nodes, breast, thyroid, salivary glands, and skin thus eliminating the need for unnecessary surgical interventions such as open biopsies.[4,5,6] Tuberculosis is one of the oldest diseases known to mankind, is caused by the acid-fast bacillus Mycobacterium tuberculosis, which is considered one of those infectious diseases responsible for causing the most deaths worldwide.[7] As stated by the World Health Organization (WHO) in the Global Tuberculosis (TB) report of 2018, approximately 10 million new cases have emerged throughout the world with 1.3 million deaths (among non-HIV patients) and 300,000 deaths among Human immunodeficiency Virus (HIV)-infected people.[8] Pakistan has been listed as one of the 8 countries which account for two-thirds of tuberculous infections worldwide with a burden of 5% (267 per 100,000) of the global incidence[8]. As of 2016, the prevalence in Pakistan is 630,000 cases (364/100,000 individuals)[9] and the incidence rate is 231/100,000.[10] The burden of TB is increasing in Pakistan due to multiple factors such as poor socioeconomic background, inadequate healthcare facilities, lack of education and awareness, overcrowding with unhygienic living conditions and shortage of rehabilitation programs after natural disasters.[9] Hence, in a developing country where the disease is endemic the time-consuming and expensive traditional methods need to be replaced with faster and cheaper diagnostic techniques, such as FNAC which is widely available, for prompt diagnosis and timely treatment.[11] TB most commonly affects the lungs but also involves other organ systems[12.] Extrapulmonary Tuberculosis is classified as infection of M. tuberculosis that involves tissues and organs apart from the lungs[13,14.] The common sites for the manifestations of Extrapulmonary TB (EPTB) are lymph nodes, pleura, genitourinary system, the gastrointestinal tract, bones and the central nervous system[15.] Approximately 15-20% of all tuberculosis cases are extrapulmonary (EPTB) while in patients with coexisting TB and HIV almost 50% of cases suffer from EPTB. The most common manifestation of EPTB is lymphadenopathy, constituting up to 50% of EPTB cases.[16] Tuberculous lymphadenitis most frequently affects the cervical lymph node group which is followed by the mediastinal, axillary, mesenteric, portal, peri-hepatic and inguinal lymph nodes respectively[17]. About 78.63% of all patients presenting with cervical lymphadenopathy are diagnosed with EPTB.[16] It clinically presents as a growing, painless lump in a group of lymph nodes. Lymph node swelling is a common presenting complaint affecting patients of all ages and

sexes. Lymph node tissue samples are used for staining, culture and cytology for a reliable diagnosis of TB lymphadenitis.[11, 18] The purpose of this study was to observe the most common diagnosis after performing FNAC in patients presenting with lymph node swellings in the outpatient department in patients of both genders and all age groups.

MATERAIL AND METHODS

In this cross-sectional study 297 patients were recruited by consecutive sampling from the rural areas of Sindh including Larkana, Ratodero, Sukkur, Shikarpur and nearby areas., All the samples were collected from the different laboratories registered in these areas from "February 2019" to "December 2019" after discussing the study with the consultant pathologist working at the sites. The registered clinical laboratories not only cover the major areas of the cities included but also covers the small villages comes around as these there are few histopathologist that work there for specific dates assigned to them. FNAC was performed in each patient after observing all aseptic measures; slides were prepared and evaluated by a panel of consultant histopathologists working in selected laboratories. A written proforma was filled to obtain a detailed history from all patients regarding the necessary clinical and pathological variables after taking the written informed consult at the time of sampling. All the data gathered was entered in the SPSS version 22. Quantitative data was represented by Mean and Standard Deviation while the qualitative data was represented by frequency and percentages. Chi square test was used to determine the association of different clinical variables with the diagnosis.

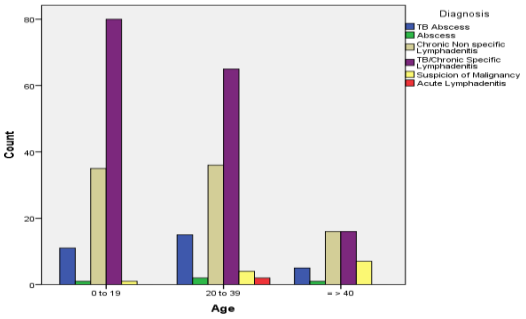
RESULTS

We enrolled 297 cases that presented with lymph node swelling of different groups and were advised FNAC in outpatient department. FNAC was performed on all patients after observing all aseptic measures; the slides were prepared and examined by histopathologists. Test results were obtained from the patients and pro-forma was filled. Of these 297 patients, 113 (38%) were males and (184) 62% were females. The ages of the subjects ranged from 1 -75 years that was divided into three respective groups, (0-19 years, 20-39 years and ≥40 years). Majority of the patients (128, 43.1%) fell in the 0-19 age group, followed by 124 (41.8%) patients with 20-39 age group and only 45 individuals (15.2) were ≥40 years of age. Table: 1

Table: 1 Frequency of study subjects and parameters included in study

Parameter	Frequency (n= 297)
Gender	
Male	113 (38%)
Female	184 (62%)
Age (years)	
0-19	138 (43.1%)
20-39	124 (41.8%)
>=40	45 (15.2%)
Site	
Left Axillary	5 (1.7%)
Right Supra Clavicular	4 (1.3%)
Submental	10 (3.4%)
Left Post auricular	2 (0.7%)
Right Post auricular	2 (0.7%)
Right Axillary	12 (4%)
Left Cervical	92 (31%)
Right Cervical	135 (45.5%)
Left Inguinal	7 (2.4%)
Right Inguinal	8 (2.7%)
Left Submandibular	7 (2.4%)
Right Submandibular	7 (2.4%)
Left Supra Clavicular	6 (2%)
Diagnosis	
TB Abscess	31 (10.4%)
Inflammatory Abscess	4 (1.3%)
Chronic Nonspecific Lymphadenitis	87 (29.3%)
TB/Chronic Specific Lymphadenitis	161 (54.2%)
Suspicion of Malignancy	12 (4%)
Acute Lymphadenitis	2 (0.7%)

The most common site of lymph node involvement was observed to be cervical group with a total of 227 cases, of which 135 (45.5%) affected the right cervical group and 92 (31%) affected the left cervical group. This was followed by the right axillary group with 12 cases (4%) and the sub-mental group with 10 cases (3.4%). A sum of 192 cases was diagnosed with granulomatous inflammation by the histological findings, out of which 161 (54.2%) cases were TB/Chronic Specific Lymphadenitis and remaining 31 (10.4%) were of TB abscess. The next common lesion observed was Chronic non-specific lymphadenitis with 87 cases (29.3%). Only 12 cases (4%) were Suspicious of Malignancy. On analyzing the results, we found no significant association between diagnosis and gender (p value= 0.137) However, females presenting with Chronic lymphadenopathy diagnosed as TB Lymphadenitis were higher in number as compared to males (female 68.9%, males 31.1%). Figure: 1A significant association was observed between the cause of lymphadenopathy and the age of the



patient (p value= 0.002) 48.4% of patients diagnosed with TB abscess fell in the age group of 20-39 years followed by 35.5% in the group 0-19 years. Of those individuals diagnosed with TB lymphadenitis 49.7% were 0-19 years of age followed by 20-39 years of age with 40.4%. Moreover, it was also seen that the diagnosis was positively associated with the site of lymph node involved (p value=0.002). TB abscess and TB Lymphadenitis were seen most commonly in the cervical lymph nodes, specifically the right cervical lymph nodes (TB Abscess; 35.5%, TB Lymphadenitis; 54%) followed by left cervical lymph nodes (TB Abscess; 32.3%, TB Lymphadenitis; 32.9%) respectively. Table: 2

Table: 2 Statistical estimates and its association with diagnosis

Characteristic	n=297	Diagnosis						p-value
		TBA	**IA**	**CNSL**	**TBL**	**SOM**	**AL**	
AGE								
0-19 Years	128	11	1	35	80	1	0	
20-39 Years	124	15	2	36	65	4	2	0.002[b]
> =40 Years	45	5	1	16	16	7	0	
GENDER								
Male	113	15	2	38	50	7	1	0.137[b]
Female	184	16	2	49	111	5	1	
SITE								
Left Axillary	5	2	0	3	0	0	0	
Right Supra Clavicular	4	0	0	1	2	1	0	
Submental	10	0	1	8	1	0	0	
Left Post auricular	2	1	0	1	0	0	0	
Right Post auricular	2	0	0	2	0	0	0	
Right Axillary	12	2	1	0	8	0	1	0.002[b]
Left Cervical	92	10	0	24	53	5	0	
Right Cervical	135	11	1	32	87	3	1	
Left Inguinal	7	0	1	2	3	1	0	
Right Inguinal	8	0	0	5	2	1	0	
Left Submandibular	7	1	0	5	1	0	0	
Right Submandibular	7	2	0	4	0	1	0	
Left Supra Clavicular	6	2	0	0	4	0	0	

[b]Pearson Chi Square
TBA=Tuberculous Abscess, IA=Inflammatory Abscess, CNSL=Chronic nonspecific lymphadenitis, TBL=Tuberculous lymphadenitis, SOM=Suspicious of Malignancy, AL=Acute Lymphadenitis

DISCUSSION

The role of fine needle aspiration cytology (FNAC) in investigating lymphadenopathy is widely accepted as a result of extensive research[19.] Some of the reasons for its abundant use in the outpatient department include minimal chances of trauma, safety and it does not require much training. Not only is it a relatively simple procedure but it is also less painful for the patient with almost no recovery time needed[1, 20]. Due to its accuracy and cost effectiveness it has become the top choice for investigation of granulomatous conditions as well as other differentials[19.] Although FNAC-based data is useful for pre-operative decisions by surgeons, it still has significant limitations, especially when it comes to distinguishing between infections and carcinomas.[21] In spite of its limitations, FNAC technique is the most commonly used FNAC is helpful in primary management of the many diseases, therefore, commonly being applied in Pakistan just like other countries of the world.[21] A study conducted in India in 2016 claims that the specificity of FNAC is 88 % and the specificity is 96%.[22]

The FNAC can access enlarged lymph nodes, which are crucial for diagnosing secondary or primary cancers. Due to its low cost, ease of use, and few complexities, it is very important in developing nations like India.[23] Especially in situations of advanced cancers, the diagnosis provided on the cytological material is frequently the only diagnostic accepted, and there is occasionally no additional association with histopathology. Additionally, it offers hints for occult primary and occasionally surprises the physician who does not have a malignancy suspicion.[24] In our analysis, malignant diagnoses were made for 4% of the lymph node FNACs. According to other studies, the incidence ranges from 5.8 to 25.03%.[25, 26.] However, among 150 cases of malignancies identified by lymph node FNAC, 102 cases (68%) of metastases and 42 cases (32%) of lymphomas were reported in an earlier Indian study.[27] Whereas: 79.4% of lymph node metastases and 14.2% of lymphomas were identified in a Brazilian investigation.[28]

The results showed that TB lymphadenitis was more common in females (68.9%) as compared to males (31.1%). This was consistent with two studies conducted in India and one in Pakistan[11, 29]. Pragati et al. in their study suggest that female predominance can be due to the influence of hormones on the immune system as an underlying cause in women. There is a greater economic dependency and illiteracy among women in underdeveloped countries making healthcare more inaccessible[24]. Furthermore, in low socioeconomic backgrounds poor nutritional status of women as compared to men further affects their immune response to disease.[29] A study also suggests that due to cosmetic reasons women are more likely to attend a healthcare facility much earlier as compared to men who would ignore a swelling until it has advanced enough to be symptomatic.[29]

In the present study the majority of patients diagnosed with TB lymphadenitis were in the first and second decades of life whereas those patients with TB abscess were most commonly in their 3rd and 4th decades. These results are congruent with a study conducted in Pakistan in 2018 according to which the majority of TB cases were below age 40[30.] Kamla et al in India also reported the most common age group for TB lymphadenitis to be 13-21 with a mean age of 23.6 years, a figure which is close to this study's mean age (24.23 years)[31.] The exact reasons for prevalence in young adults is not clear but

some possible explanations in a highly endemic country like Pakistan could be lack of awareness or misinformation regarding vaccinations as well as failure to comply with the entire EPI schedule. Moreover, poor hygienic conditions, overcrowding and malnutrition hinder the development of a strong immune system. Globally, adolescence and young adulthood is recognized as being a risk factor for TB infections and transmissions as well as increased chances of adverse outcomes. This is because this age group is more prone to social interactions and substance abuse[32.]

In the current study the most frequently affected groups were the cervical groups (right cervical 45.5%, left cervical 31%). This was followed by axillary lymph nodes (right axillary 4%, left axillary 1.7%) however; there was a sizeable difference between the frequencies of the two presenting sites. Cumulatively, tuberculous lymphadenitis and tuberculous abscess were most prevalent. Niaz Hussain Soomro et al, in a 2016 study, reported the cervical region as the most common site for EPTB. However, axillary and inguinal sites were also seen[33.] A similar finding was observed in our study where the highest numbers of individuals presenting with cervical lymph node swellings were diagnosed with TB. A previous study concluded that TB lymphadenitis is the most common diagnosis in superficial neck swellings proceeded by non-specific inflammation and neoplasms[1.]

CONCLUSION

FNAC is the most commonly used technique to investigate swellings of lymph nodes and the commonest cause of cervical lymphadenopathy is attributed to TB. Therefore, it is imperative to use FNAC as one of the initial investigations to rule out tuberculous lymphadenitis in all cases presenting with lymph node enlargement. In current survey female of younger age groups were more frequently presented with right cervical lymphadenophies having the chronic non specific lymphadenitis. Age and site of lymph node involved had association with the diagnosis of FNAC.

Strengths: Hence, the results of this study should be considered for changes in the national TB policies to focus on prevention, early diagnosis and treatment in this particular age group [(23)].

ETHICS APPROVAL: The ERC gave ethical review approval. REFF: 4210921AAPATH DATED: 04/11/2018.

CONSENT TO PARTICIPATE: written and verbal consent was taken from subjects and next of kin.

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