RETROSPECTIVE ASSESSMENT OF THE PREVALENCE OF TUBERCULOSIS FINDINGS AMONG PAEDIATRIC PATIENTS REFERRED FOR COMPUTED TOMOGRAPHY SCAN AT PORT MORESBY GENERAL HOSPITAL, PAPUA NEW GUINEA

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ABSTRACT:

Tuberculosis (TB) is a major cause of death among all people worldwide. TB is prevalent in the developing countries resulting in deaths. Papua New Guinea (PNG) is a developing country that is greatly affected by TB, particularly paediatric TB. This study is a retrospective assessment of TB findings among paediatric patients referred for computed tomography (CT) scan at the Port Moresby General Hospital (PMGH) over a period of 24 months (January 2019 to December 2020). The case files of all the paediatric patients were collected from the CT register books after obtaining ethical clearance. The relevant information was recorded in Excel Spread sheet. The data was statistically analysed using Microsoft Excel 2013. A total of 234 TB findings were recorded. Of these, space occupying lesions (SOL) (71%) was the prevalent finding identified more frequently compared to tuberculoma (22.6%) and TB meningitis (TBM) (6.4%). The highest number of cases was among children in the 3 to 11 years' age group. We cannot conclude that SOL is the common TB findings in PNG currently, because no standardized data recording is available and CT data alone is not relevant as most paediatrics preferred non-ionising radiation.

Keywords: tuberculosis, tuberculoma, space occupying lesion, tuberculosis meningitis, paediatric, computed tomography, Papua New Guinea

INTRODUCTION:

Tuberculosis (TB) is a communicable disease that is one of the top 10 causes of death worldwide and the leading cause of death from a single infectious agent [1]. TB is caused by the bacillus *Mycobacterium tuberculosis*, which is spread when people who are sick with TB expel bacteria into the air; for example, by coughing [1]. The 2004 Priority Medicines Report stated that TB is a major and growing threat to public health for Europe and the world, with new epidemiological challenges [2]. In

2020, the World Health Organisation (WHO) estimated that 10.0 million of the world's population were infected with TB and an estimated 1.2 million deaths from TB occurred in the world with 87% of all cases in 22 countries, mainly in South-East Asia (44%), Africa (25%) and the Western Pacific (18%) [1]. In that year, children (aged <15 years) accounted for 12% of the population with TB cases. It is however important to note that TB is curable and preventable. About 85% of people who develop TB disease can be successfully treated with a 6-month drug regimen; treatment that has the additional benefit of curtailing onward transmission of infection [1]. However, non-compliance of the 6-month TB drug regimen may result in drug-resistant TB (DR-TB), which continues to be a global public health threat [1]. Although the global incidence rate of TB is falling, it is not fast enough to reach the 2020 milestone of a 20% reduction between 2015 and 2020 [1].

Incidence of TB in Papua New Guinea [PNG]:
At present, TB incidence has more impact on low-and-middle-income countries (LMICs) than high-income countries [2]. PNG, a LMIC, is located in the Western Pacific Region and is categorised as one of the areas in the world that have high incidence of TB [1]. A recent epidemiology study carried out in PNG involved analysis of TB cases and treatment outcomes using routine surveillance data from the

national TB database for the period 2008-2016 [3]. The study reported that the case notification rate for all forms of TB in PNG was 333 per 100 000 of the population. Interestingly, the proportion of paediatric TB in PNG (26.7%) was found to be higher than other high-burden countries in the Western Pacific Region [3-5]. This proportion was higher than the global estimate of 12% of all TB cases [1], and the highest proportion of TB cases in children reported globally [6]. Paediatric TB remains a public health emergency and this is particularly evident in LMICs countries such as PNG with poor public health infrastructure [7].

Patterns of paediatric central nervous system TB:
The natural history of TB in children and paediatrics follows a series of 5 steps in which phase 1 occurs after an incubation period of 3-8 weeks after primary infection and phase 5 occurs up to 3 years after phase 1 [7]. After primary infection, the regional nodes enlarge and organisms escape into the blood stream [8]. Extrapulmonary TB or miliary TB is a complication of primary TB in young children which includes peripheral lymphadenopathy, TB meningitis, skeletal TB, and other organ involvement [7]. TB commonly affects the lungs and when not treated early, it may spread to other parts of the body, mainly the brain and the spinal cord which are referred to as central nervous system (CNS) TB. CNS TB occurs in

approximately 1% of all patients with active TB, and is the most lethal complication of TB in developing countries [9]. The four main patterns of CNS TB include: tuberculous meningitis (TBM); tuberculomas in brain and spinal cord (TBT); tubercular brain abscess (TBA); and tuberculous encephalopathy (TBE) [10]. TB of the CNS may present in 3 different ways including meningitis, encephalitis and as a space occupying lesion (SOL) [8]. The commonest cause of SOL in children in most tropical countries is tuberculoma (in up to 50% of cases) [8]. Tuberculoma is caused by mycobacterium TB (MTB) that results in a caseous mass encapsulated by multiple concentric layers of connective tissue without surrounding inflammation or spread [11-13]. Tuberculomas account for up to 40% of brain tumours in some areas of the world [11], while in developing countries, the incidence of tuberculoma varies from 5% to 30.5% of all intracranial SOLs [13]. Intracranial tuberculomas occur in 13% of children with neurotuberculosis [9]. TBM is the most fatal form of TB and the incidence varies from 1% to 5%, affecting mainly children under 5 years of age [14-15].

Paediatric Age Category and TB Diagnosis in Medical Imaging:

The WHO published pediatric-specific disease estimate for the first time in 2012 reported that approximately 500,000 cases of TB among children are younger than 15 years of age [16]. Children and young adults are categorised under paediatric. According to US Food and Drug Administration, paediatric patients are defined as aged up to 16 years only and are categorised into four different groups which include the following: (1) Neonates: age group 0 to 1 month; (2) Infants: age group 1 month to 2 years; (3) Children: age group 2 to 12 years; (4) Adolescents: age group 12 to 16 years [17]. Clinical assessment, laboratory testing and chest radiograph are used to confirm the diagnosis for TB [5]. In medical imaging, different modalities can be used to identify TB depending on its location. In the case of CNS TB, the two imaging modalities used are Magnetic Resonance Imaging (MRI) and Computed Tomography (CT) [11].

TB remains a public health problem with lethal CNS complications in developing countries [14]. PNG is a developing country with a growing population of over seven million [18-20] and is considered to have a high prevalence of paediatric TB cases [3, 5-6]. In PNG, there are twenty-two provinces and the National Capital District (NCD) in four administrative regions. The rural areas of PNG comprise a higher population of 87.5%, whilst only 12.5% of the populations live in urban areas and about 400,000 people (4.5%) live in the capital Port Moresby [18-20].

There are no published studies on the prevalence of TB findings among pediatric patients and its diagnosis using CT scan in PNG.

The major objective of this study was to retrospectively assess TB findings among paediatric patients referred for CT scan at the PMGH over a period of 24 months (January 2019 to December 2020).

METHODOLOGY:

This was a descriptive study with convenience sampling conducted at PMGH Radiology Department [21-23]. The PMGH is the major public general, specialist and reference hospital in the National Capital District (NCD) and PNG offering level 7 medical services [23]. It is also the teaching hospital for the School of Medicine and Health Sciences (SMHS), University of Papua New Guinea (UPNG). The patients represent a cross-section of the NCD population and the Central Province [23].

Cases of paediatric patients with TB findings were collected retrospectively from the CT record book from January 2019 to December 2020. The variables collected were age, gender and findings associated with TB. The data were recorded in Microsoft (MS) Excel Spreadsheets.

Patients whose age ranged above 17 years and did not present with TB findings were excluded in this study. Patients' cases files that did not record the specific age and cases from other imaging modalities were also excluded from the study. A total of 278 TB findings were recorded. Of these, 44 (15.8%) cases were excluded from the study due to age above 17 years, did not present with TB findings, no recorded age and were diagnosed using other imaging modalities. Thus, a total of 234 cases were suitable for analysis. The data for the 234 cases was analysed statistically using the MS Excel Spreadsheets data pack version 2013.

Ethical approval for this study was granted by the School of Medicine and Health Science Research and Ethics Committee (SMHS REC). Written consent was granted by the Director of Medical Service at PMGH with the approval from the Head of Radiology Department.

Criteria for data analysis by paediatric age groups: Four categories of paediatric age groups were used in the present study [17]. Neonate: 0 to 1 month. Infant: 2 months to 2 years. Children: 3 to 11 years. Adolescence: 12 to 16 years.

RESULTS:

Over the duration of 24 months a total of 278 cases with TB findings were recorded in the CT record book in PMGH. However, because of the exclusion criteria in the present study only 234 (84.2%) TB findings were found suitable for analysis. Table 1 shows the distribution of all the paediatric patients according to gender

and age groups. In the present study, 137 males (58.5%) and 97 females (41.5%) were examined. The age range for all patients was from 2 months to 16 years.

The prevalence of TB findings was highest (68.4%) among those in the 3 to 11 years' age group. There was equal distribution of TB findings among those in the 12 to 16 years' age group and 2 months to 2 years' age group with 15.8% each. There was no recorded distribution of TB findings among neonates from birth to 1 month.

TB findings identified in paediatric patients:

Three common TB findings were recorded among the patients. Space occupying lesion (SOL) (71%) was the prevalent finding that was identified more frequently compared to the others. This was followed by tuberculoma (22.6%), and TB meningitis (TBM) (6.4%) was the very least finding identified among the 234 patients (Table 2).

TB findings according to age category:

In terms of the distribution of TB findings among different age groups, the results reveal that children had the highest distribution of SOL (71.7%), followed by infant (14.5%) and adolescence (13.9%). Tuberculoma was the second common finding among children

(58.5%), followed by adolescence (24.5%) and infants (17%). TBM was common among children (73.3%) and infants (26.7%). There was no recorded distribution of TBM among the adolescence while neonates recorded no distribution of all three TB findings (Table 3).

TB findings of male versus female paediatric patients according to age categories and gender:

Table 4 shows the distribution of TB findings according to age category and gender. The results reveal that male children had the highest distribution of SOL (43.4%), TBM (60%) and tuberculoma (37.7%) compared to female at 28.3%, 13.3% and 20.8%, respectively. Among the infants, the percentage distribution of TBM (20%) and tuberculoma (13.2%) were higher among the female patients compared to male patients at 6.7% and 3.8%, respectively; while male patients have high percentage of SOL (9%) compared to female (5.4%). In adolescence, females have higher distribution of tuberculoma (15.1%) compared to males at 9.4%; while males have slight higher frequency of SOL (7.8%) compared to females (6%). There was no recorded distribution of TBM among both male and female patients in the adolescence category.

Table 1: % (n) distribution of all the paediatric patients according to gender and age groups.

Age groups	Males % (n = 137)	Females % (n = 97)	Total % (n = 234)
12 - 16 years	13.1 (18)	19.6 (19)	15.8 (37)
3 - 11 yeas	73.7 (101)	60.8 (59)	68.4 (160)
2 months - 2 years	13.1 (18)	19.6 (19)	15.8 (37)
0 - 1 month	0	0	0

Table 2: % (n = 234) distribution of TB findings among all the paediatric patients.

TB Findings	% (n)
Space occupying lesion (SOL)	71.0 (166)
TB Meningitis (TBM)	6.4 (15)
Tuberculoma	22.6 (53)

Table 3: % (n) distribution of TB findings according to age categories.

Age category	SOL (n = 166)	TBM (n = 15)	Tuberculoma (n = 53)
Adolescence (12 - 16 years)	13.9 (23)	0	24.5 (13)
Children (3 - 11 years)	71.7 (119)	73.3 (11)	58.5 (31)
Infant (2 months - 2 years)	14.5 (24)	26.7 (4)	17.0 (9)
Neonate (0 - 1 month)	0	0	0

Table 4: % (n) distribution of TB findings of male versus female paediatric patients according to age categories and gender.

Age category	Gender	SOL (n = 166)	TBM (n = 15)	Tuberculoma (n = 53)
Adolescence (12 - 16 years)	M	7.8 (13)	0 (0)	9.4 (5)
	F	6.0 (10)	0 (0)	15.1 (8)
Children (3 - 11 years)	M	43.4 (72)	60.0 (9)	37.7 (20)
	F	28.3 (47)	13.3 (2)	20.9 (11)
Infant (2 months - 2 years)	M	9.0 (15)	6.7 (1)	3.8 (2)
	F	5.4 (9)	20.0 (3)	13.2 (7)
Neonate (0 - 1 month)	M & F	0	0	0

DISCUSSION:

TB may affect male and female at the same rate or may affect them differently. More than half (58.5%) of all the paediatric patients with TB findings referred for CT scan in PMGH in the duration of this study were males.

Our findings are in contrast to a study by Al-Hussaini et al. who assessed the intracranial tuberculoma in different age and gender groups [24]. Their study involved cases of 291 pediatric patients (0-19 years of age) where they concluded that females were more likely to be affected in 2nd and 3rd decades of life, while males were more likely to be affected in later decades.

The present study however did not assess cases of paediatric patients above 17 years of age to predict their risk of survival from TB. In the present study, the prevalence of TB findings was highest (68.4%) among those in the 3 to 11 years' age group. This finding is consistent with evidence that among children, the greatest numbers of TB cases are seen in children less than 15 years of age [1-2, 16]. There was equal distribution of TB findings among those in the 12 to 16 years' age group and 2 months to 2 years' age group with 15.8% each in the present study.

This finding suggests that TB cases among paediatrics can be disaggregated by sex and age groups and may account for variations in incidence rates by age, sex and country [1].

TB findings identified in paediatric patients:

In the present study, space occupying lesion (SOL) (71%) was the prevalent finding that was identified more frequently compared to the others. This finding is consistent with a study done elsewhere [10] reporting that SOL associated with headache and seizures accounted for 60 to 100% of intracranial tuberculoma. This was followed by tuberculoma (22.6%), and TB meningitis (TBM) (6.4%) which was the least finding identified among the 234 patients in the present study. These findings are consistent with evidence that tuberculomas account for up to 40% of brain tumours in some areas of the world [11], while in developing countries, such as PNG, the incidence of tuberculoma varies from 5% to 30.5% of all intracranial SOLs [13]. Other similar evidence confirm that intracranial tuberculomas occur in 13% of children with neurotuberculosis [9], whilst TBM is the most fatal form of TB and the incidence varies from 1% to 5%, affecting mainly children under 5 years of age [10, 14-15]. The total number of tuberculoma cases recorded in the present study is 53 (22.6%), however this was not the actual number of cases that underwent CT examination over the duration of 24 months.

Magnetic resonance imaging (MRI) has been found to be superior to CT of the head for visualization of tuberculomas [25], however the

present study did not assess tuberculoma cases referred for MRI examination. It is well known that tuberculoma is associated with both SOL and TBM and is defined as SOL resulting from metastatic TB [10-11, 26]. This definition may imply that SOL can be used to represent tuberculoma. Therefore, the total number of tuberculoma cases in the present study may not be 53 (22.6%), however could take into account the total number of SOL (n=166, 71%) and TBM (n=15, 6.4%).

TB findings according to age category:

In terms of the distribution of TB findings among different age groups, the present study revealed that SOL is present in infants with a total of 14.5% cases and is increased to 71.7% in children and then decreases to 13.9% in adolescent. Like SOL, tuberculoma also followed the same trend. It had 17% cases in infants and then increased to 58.5% in children and later decreased to 24.5% in adolescent. TBM on the other hand, only increased in infants from 26.7% cases to 73.3% cases in children. In all three age groups, children have the highest number of all three TB findings, which suggest that tuberculoma mostly affects children [8-9] compared to those in the neonate, infant and adolescent groups. To confirm this finding, the mean age of the patients in the present study is 7 years and the median age is 6 years and mode is 6 years. This imply that the majority of paediatric cases

were around 6 and 7 years of age which falls under the children category that consist of age ranging from 3-11 years old [17]. This finding aligns with WHO published pediatric-specific disease estimate reporting that approximately 500,000 cases of TB among children are younger than 15 years of age [16]. Further evidence confirms that where there is a greater number of TB, there is also an increase in tuberculoma cases [27]. This evidence is also revealed in the present study which shows a positive relationship; meaning tuberculoma increases and decreases with its associated indications (SOL and TBM). Another interesting finding in the present study revealed that neonates recorded no distribution of all three TB findings. This does not mean that neonates are not being affected by tuberculoma. This finding confirms the evidence that neonates normally undergo different imaging modality examination because of their increase risk of developing cancer [28]. Further evidence from the American Academy of Paediatrics (AAP), confirmed that CT increases the risk of cancer especially in new-borns because their brains are still developing, whilst unnecessary CT scan examination can lead to more tests and treatments with more risks [28].

TB findings according to age categories and gender:

The present study shows the distribution of TB findings according to age category and gender.

Overall, the ratio of a male to female is 1.4:1 which implies that the males were affected more than the females over the duration of 24 months. This finding differs with a study done by Al-Hussaini et al. [24] on the assessment of intracranial tuberculoma in different age groups and the method used for diagnosis. The same study was based on 291 cases where the result showed that the male and female were affected almost equally with a male to female ratio of 1:1.03. In contrast, the ratio of tuberculoma among male and female children in the present study is 1.8:1 which implies that male children were affected more with tuberculoma than the female children, while male adolescence and male infants were least affected with tuberculoma than their female counterparts with a ratio of 1:1.6 and 1:3.5, respectively.

Limitation of the study:

Since CT uses ionizing radiation, it is not recommended for neonates. This may influence the recorded cases of TB findings for neonates.

CONCLUSION:

The results of the present study revealed that SOL (71%) was the prevalent finding identified more frequently compared to tuberculoma (22.6%) and TBM (6.4%). Tuberculoma is associated with SOL and TBM. Overall, males were affected more than females with a ratio of 1.4:1 over the duration of 24 months. Male

children were affected more with tuberculoma than the female children with a ratio of 1.8:1, while male adolescence and male infants were least affected with tuberculoma than their female counterparts with a ratio of 1:1.6 and 1:3.5, respectively. Among paediatrics, the most affected age group is children (3 to 11 years). We cannot conclude that SOL is the common TB findings in PNG currently, because no standardized data recording is available and CT data alone is not relevant as most paediatrics preferred non-ionising radiation.

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