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Research Article

Assessment of Prevalence of Drug Resistant Tb in Kasama

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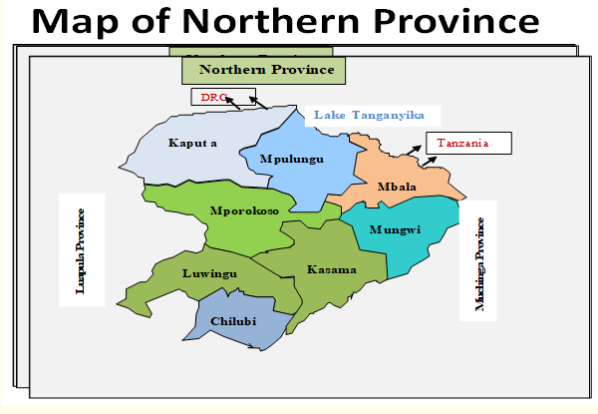

Figure 1

Abstract

- To assess the prevalence of drug resistant tuberculosis in kasama district between June 2017 and June 2018.
- To determine the proportion of new TB cases in Kasama district that has resistance to selected first-line anti-tuberculosis drugs.
- To determine the proportion of previously treated cases in kasama district that has resistance to selected first line anti-tuberculosis drugs.
- To evaluate associations between drug resistance and age groups and sex in kasama district.
- To evaluate associations between tb drug resistance and HIV status in kasama district.
- To assess diagnostic platforms for diagnosing drug resistance tuberculosis in kasama district.
- To isolation facilities for multidrug resistance suspects in Kasama district.

A retrospective prevalence study was conducted to assess and understand the DR-TB situation in Kasama district to ascertain the magnitude of the problem and to discuss possible mitigation issues to improve DR-TB control efforts and patient management, strengthen surveillance data in health facilities to inform policy makers and to provide baseline data for measurement of program achievements.

Keywords: Assessment of Prevalence; Drug Resistant

Introduction

The burden of tuberculosis (TB) in Zambia is among the highest in the African region and in 2013 the prevalence was estimated at 388/100,000 population according to the World Health Organization (WHO) and an estimated incidence rate of 427/ 100 000 population; TB is one of the major public health problems in the country with a notification rate of 289/ 100 000 population of all forms of TB in 2012. Zambia was one of the 22 high priority countries selected by the World Health Organization (WHO) to undertake a national TB prevalence survey [1-3], because it met the criteria as defined by the WHO Global Task Force on TB Impact Measurement [4]. Historically, there have been no national TB prevalence surveys that have been conducted in Zambia. Therefore, the country lacked baseline data on the prevalence of tuberculosis disease (TB). The WHO recommends implementation of population-based prevalence surveys to estimate the prevalence of TB for baseline and consequently impact assessment to measure progress [3,4]. The prevalence of MDR TB, in new patients is estimated at 1.8% and 2.3% in previously treated cases, based on the 2001 Drug Resistance Survey. This translates in approximately 265 new cases of MDR TB in Zambia each year. Currently the National TB control Programmed is recording a number of confirmed MDR TB cases from selected parts of the country. Appropriate management of MDR TB cases would allow the NTP to achieve good cure rates and at the same time reduce the risk of transmission of resistant strains [5] The TB/HIV co-infection, is an important factor to take into account in the management of MDR TB.

In sub-Saharan Africa, DR-TB surveillance data have been scarce in the past years and few countries have conducted drug resistance surveys (Wright., *et al*. 2009; [6] WHO 2010; [7] Zignol., *et al*. 2012a) [8]. The limitation is mainly due to inadequate diagnostic capacity and drug susceptibility testing (DST) in most sub-Sahara African countries (Wright., *et al*. 2009) [6,9]. Zambia has made good progress in tuberculosis (TB) control with the estimated prevalence rates showing a downward trend and having very good treatment outcomes in new cases and retreatment cases regardless of the HIV status of the patients (Kapata., *et al*. 2012; WHO 2012b) [10,11].

In Zambia, TB is mainly diagnosed by microscopy, using Ziehl–Neelsen (ZN) stains (Kapata., *et al*. 2011); [12] culture and DST have been performed in Zambia since the late 1990s, although there are currently no reliable records and reports on this before the year 2000. Initially, routine culture and DST were only performed at the National Reference Laboratory (NRL), which catered for the whole country. The capacity to perform culture and DST gradually increased from one referral centre (NRL) to three by the year 2008, which included the University Teaching Hospital (UTH) and the Tropical Diseases Research Centre (TDRC). These laboratories cater for a population of approximately 13.4 million across a land surface area of about 752 000 square kilometers.

It was only recently between 2014 and 2017 that Zambia has scaled up molecular testing for diagnosing tuberculosis using Gene expert diagnostic platform in certain districts of the country of which Kasama has only three (3) Gen expert located at the general hospital, location clinic and Chishimba Zambia national service.

Therefore, we conducted a retrospective assessment to understand the Drug resistant-TB situation in Kasama district to ascertain the magnitude of the problem and to discuss possible mitigation issues to improve drug resistance TB control efforts and patient management.

Statement of the problem

Currently, kasama district health office is relying on routine surveillance data from health facilities collected through the national TB control program, to measure progress towards TB control targets. This data has limitations such as under-reporting, and it does not provide information on the number of undetected cases in the community and on those individuals seeking care outside of the public sector, the burden in kasama is not well defined because routine surveillance data are scarce. An inadequate drug resistant diagnostic platform in the districts, and or the distance between each Gen Expert machine is a concern. The platform itself seems inadequate as it can only do 12 sputa per technician's shift per day against high workload of 25 samples per day. The HIV pandemic and poverty in the Country may have also led to increase in the TB burden; furthermore, routine surveillance data may have gaps due to recording and reporting bias [4,13]. Even for those that have the resistant strain are there isolation facilities to accommodate them or we have left them to infect others?. Therefore, a Kasama district representative population-based survey will be conducted to estimate the burden of disease to inform policy makers and to provide baseline data for measurement of program achievements.

Rationale/justification of the statement of the problem

Drug-resistant tuberculosis diagnosis strategy looks at the diagnosis of drug-resistant TB (DR-TB) and MDR-TB made by collecting

sputum samples from the suspected patients and subjecting the specimen to culture on either solid media using Löwenstein–Jensen (LJ) or on liquid media using Mycobacteria Growth Indicator Tube (MGIT) and then performing drug susceptibility testing on the positive samples for rifampicin and or isoniazid. The suspected DR-TB patients are usually the patients who fail first-line treatment and have sputum smear-positive results at three to 5 months of treatment and at the end of treatment; all retreatment cases are also considered to be DR-TB suspects. It will be important not only to underscore the prevalence of either mono resistance or multidrug resistance but also to bring out recommendations about the inadequate diagnostic platforms for DR-TB, Isolation facilities if any, strengthen surveillance data in health facilities to inform policy makers and to provide baseline data for measurement of program achievements.

Methodology

Research design

A survey approach was used in conducting this research. A quantitative and or qualitative method of data collection was employed to yield empirical data to compliment the qualitative data.

This was a cross sectional retrospective prevalence study using checklist for health facility data which included lab registers, treatment registers, and district quarterly reports for the period between June 2017 to June 2018.

Sampling strategy

100% sampling method was suitable due to relatively small numbers of TB diagnostic units in the district. All eligible patients enrolled at each diagnostic Centre within the same limited intake period were included. The self-weighted character of this design ensured by the inclusion of all diagnostic centres and by the use of the same enrolment period for each of them.

Research instruments

These referred to tools that were used in collecting the necessary data, these included:

- Observational checklist: facility, registers both lab and treatment.

Data collection

This refers to the gathering of information to answer research questions.

- Observation guide was used to collect information from health workers/specialists.
- Registers, reports etc.

Data analysis

The data processing phase for this survey typically involved the classification of the written in answers and transformation of all information to some computer format either on magnetic discs, flash discs or computer hardware disk, therefore SPSS V 16.0 was used.

In this study inferential analysis was used to draw conclusions concerning the relationships and differences found in the research data eg frequencies.

Interpretive techniques that were used include observer impression for the qualitative components and the coding which both organized the data and provided a means to introduce the interpretation of it into certain quantitative methods.

Findings

According to the proposal research questions the following were the findings:

To determine the proportion of new TB cases in Kasama district that has resistance to selected first-line anti-tuberculosis drugs.

	Frequency	Percent	Valid Percent	Cumulative Percent
	1	.3	.3	.3
No data	7	.3	.3	1.0
No Results	3	1.0	1.0	1.9
Positive	298	92.5	92.5	100.0
Total	308	100.0	100.0	

Table 1: Frequency table Showing diagnosis results.

		Frequency	Percent	Valid Percent	Cumulative Percent
Valid		1	.3	.3	.3
	Neg2,5	204	66.2	66.2	66.9
	Neg2, pos 5	1	.3	.3	67.2
	not done	71	20.1	20.1	89.0
	pos@2	17	3.9	3.9	94.5
	pos@5	6	1.6	1.6	96.8
	pos2, neg 5	7	1.0	1.0	98.7
	Total	308	100.0	100.0	

Table 2: FOLLOW-UP Smear Results.

Total SM+@2month+5month/Total SM+@diagnosis x100
31/298x100=10.7%
The prevalence rate of primary resistance
Total SM+@2months 24/298X100=8.3%

To determine the proportion of previously treated cases in kasama district that has resistance to selected first line anti-tuberculosis drugs.

The prevalence rate of secondary resistance
Total SM+@5monthsx8/298X100 = 2.6%

The prevalence rate of Multidrug resistance
Total RR+Treatmentfailure/Total Sm+ve X100
7/298x100 = 2.3%

The prevalence rate of Rifampcin drug resistance
4/298x100= 1.3%

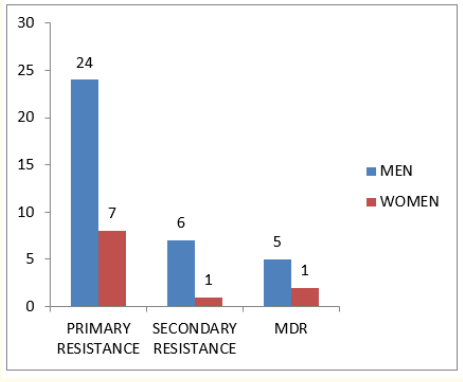

Figure 2: Prevalence by gender.

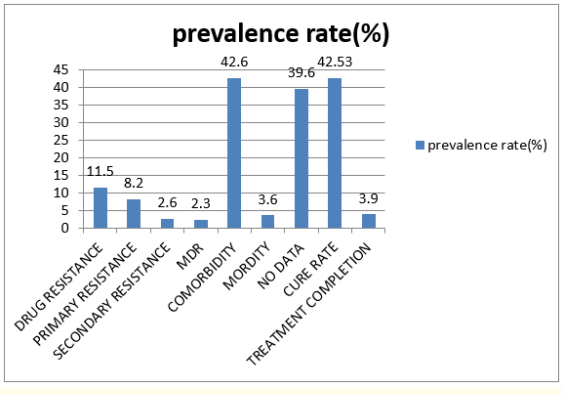

Figure 3: Shows Prevalence Rate from (i, ii, iii, iv, v, vi, vii, viii, ix).

Rate of non-evaluation of treatment outcomes
122/308x100=39.6%

Cure rate
131/308x100=42.58%

Treatment completion rate.
10/308x100=3.2%

The ratios of comorbidity by sex and age.

		Frequency	Percent	Valid Percent	Cumulative Percent
Valid		1	.3	.3	.3
	Comp treatme	10	1.6	1.6	1.9
	Cured	131	42.5	42.5	44.5
	Died	11	.3	.3	48.1
	Lost follow up	3	.6	.6	48.7
	NO Data	119	3.9	3.9	87.3
	TO	25	8.1	8.1	96.4
	Treat Failure	6	1.3	1.3	99.7
	Treatmen-tReSt	1	.3	.3	100.0
	Total	308	100.0	100.0	

Table 3: Showing Treatment Outcomes, Frequency.

	Frequency	Percent	Valid Percent	Cumulative Percent
Valid	104	33.8	33.8	33.8
12	1	.3	.3	34.1
13	1	.3	.3	34.4
17	3	1.0	1.0	35.4
18	2	.6	.6	36.0
19	3	1.0	1.0	37.0
20	3	1.0	1.0	38.0
21	2	.6	.6	38.6
22	11	3.6	3.6	42.2
23	3	1.0	1.0	43.2
24	2	.6	.6	43.8
25	9	2.9	2.9	46.8
26	2	.6	.6	47.4
27	6	1.9	1.9	49.4
28	7	2.3	2.3	51.6

29	2	.6	.6	52.3
3	1	.3	.3	52.6
30	7	2.3	2.3	54.9
31	6	1.9	1.9	56.8
32	6	1.9	1.9	58.8
33	3	1.0	1.0	59.7
34	4	1.3	1.3	61.0
35	10	3.2	3.2	64.3
36	2	.6	.6	64.9
37	7	2.3	2.3	67.2
38	8	2.6	2.6	69.8
39	5	1.6	1.6	71.4
40	9	2.9	2.9	74.4
42	9	2.9	2.9	77.3
43	2	.6	.6	77.9
44	5	1.6	1.6	79.5
45	3	1.0	1.0	80.5
46	4	1.3	1.3	81.8
47	1	.3	.3	82.1
48	2	.6	.6	82.8
49	3	1.0	1.0	83.8
50	1	.3	.3	84.1
52	1	.3	.3	84.4
54	2	.6	.6	85.1
55	1	.3	.3	85.4
56	1	.3	.3	85.7
57	1	.3	.3	86.0
58	1	.3	.3	86.4
59	1	.3	.3	86.7
60	2	.6	.6	87.3
61	1	.3	.3	87.7
65	1	.3	.3	88.0
67	1	.3	.3	88.3
69	1	.3	.3	88.6
71	1	.3	.3	89.0
73	1	.3	.3	89.3
76	1	.3	.3	89.6
77	1	.3	.3	89.9
8	1	.3	.3	90.3
81	1	.3	.3	90.6
87	1	.3	.3	90.9
Female	1	.3	.3	91.2
Nodata	27	8.8	8.8	100.0
Total	308	100.0	100.0	

Table 4

	Frequency	Percent	Valid Percent	Cumulative Percent
Valid	226	73.4	73.4	73.4
1	1	.3	.3	73.7
19	2	.6	.6	74.4
20	2	.6	.6	75.0
21	1	.3	.3	75.3
22	3	1.0	1.0	76.3
23	2	.6	.6	76.9
24	1	.3	.3	77.3
25	2	.6	.6	77.9
26	2	.6	.6	78.6
27	5	1.6	1.6	80.2
28	4	1.3	1.3	81.5
29	4	1.3	1.3	82.8
30	3	1.0	1.0	83.8
31	1	.3	.3	84.1
32	4	1.3	1.3	85.4
33	4	1.3	1.3	86.7
35	3	1.0	1.0	87.7
36	5	1.6	1.6	89.3
37	5	1.6	1.6	90.9
38	1	.3	.3	91.2
39	2	.6	.6	91.9
40	1	.3	.3	92.2
43	2	.6	.6	92.9
44	1	.3	.3	93.2
45	2	.6	.6	93.8
47	1	.3	.3	94.2
48	1	.3	.3	94.5
49	1	.3	.3	94.8
50	2	.6	.6	95.5
52	1	.3	.3	95.8
53	2	.6	.6	96.4
55	1	.3	.3	96.8
56	1	.3	.3	97.1
58	1	.3	.3	97.4
60	1	.3	.3	97.7
61	1	.3	.3	98.1
62	1	.3	.3	98.4
63	1	.3	.3	98.7
77	1	.3	.3	99.0
81	1	.3	.3	99.4
85	1	.3	.3	99.7
male	1	.3	.3	100.0
Total	308	100.0	100.0	

Table 5: Showing of age and male comorbidity.

	Frequency	Percent	Valid Percent	Cumulative Percent
Valid	1	.3	.3	.3
NEW	254	82.5	82.5	82.8
NO DATA	12	1.9	1.9	84.7
RELAPSE	29	10.7	10.7	95.8
T/I	11	3.6	3.6	99.4
T/O	2			100.0
Total	308	100.0	100.0	

Table 6: Showing Patient Type.

Loss to follow up rate
3/308x100=0.97%

	Frequency	Percent	Valid Percent	Cumulative Percent
Valid	1	.3	.3	.3
No DATA	4	.6	.6	1.0
Non React	175	56.8	56.8	58.1
Reactive	128	41.6	41.6	99.7
Total	308	100.0	100.0	

Table 7: Showing HIV status.

Construct the recommendations concerning inadequate diagnostic platforms for resistant tuberculosis The average distance between the health facilities in kasama district was 11.3km apart, therefore access to the gene Expert machine is an bearable, if we are to eradicate TB by 2030,this distance must be reduced in order to increase diagnostic case finding. There was no significance in the referred samples for culture at chest diseases laboratory in Lusaka as the culture results were not available.

Determine the availability of the isolation facilities in the district and or the model for referral The study did not find any isolation facility in the district for isolation of resistant TB clients and the referral procedure was not well tabulate and some health workers were not well oriented.

Evaluate the factors in TB-HIV comorbidity in the prevalence of DR-TB.

The study showed that three factors were significant and these included and not limited to patient transfers 13/305, none initiation on HAART 59/305, none compliance to drug taking or in accessible to drugs resulting in 29/305 relapse cases were seen to acerbated the problem. None documentation in the facility registers both treatment and laboratory were a sole site, therefore if we are to combat drug resistance, for the purpose of monitoring progress towards achieving national targets documentation has to be credible.

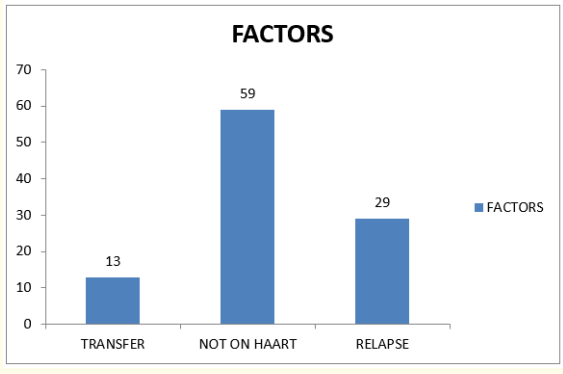

Figure 4: Shows factors leading to high comorbidity.

Figure 5: Shows the rates of type of transfer.

Rate of Morbidity

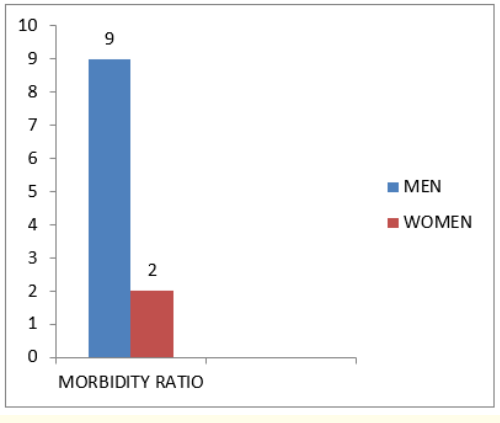

Figure 6: Shows ratio of morbidity by gender.

Discussion

Resistance can develop within four weeks with mono-therapy or treatment with inappropriate drug combinations. This is why we can safely assume that any patient who has received at least four weeks of TB therapy is no longer a "new" patient and should be managed as a patient who has been treated before and potentially has some form of TB drug resistance. The study determined the proportion of new TB cases in Kasama district that has resistance to selected first-line anti-tuberculosis at 10.7%, while the prevalence rate of primary resistance was = 8.3%. In Zambia, a national drug resistance survey was conducted in 2001, reporting the prevalence of MDR-TB to be low at 1.8% and 2.3% in new and retreatment cases, respectively (Mulenga., *et al*. 2010) [12]. The presence of drug resistance among new cases reflect creation and transmission of drug resistant strains over many years, and can be readily used to assess the quality and performance of a national TB control programmed. An established national TB control programmed that adopts standardized chemotherapy and an effective control programmed will see a subsequent reduction in drug resistance among new cases, although this may take a long time to become significant, since patients infectected with resistant strains may become ill only after many years. The high proportions of resistance among new cases may also indicate that some previously treated patients had been misclassified as new cases. This was confirmed by the high Rate of non-evaluation of treatment outcomes at 39.6%.and relapse cases at 29/308.

Young population were more likely than older people to have been recently infected, frequency table 1,4 and 5 indicated ages between 22 to 30years. And by gender more males than females seem to have been recently been infected. The proportions of drug resistance in new cases among younger age groups therefore provide more information on recent patterns of transmission of drug-resistant TB and the quality of a national TB control programmed.

In the second objective the proportion was determined of previously treated cases in Kasama district that has resistance to selected first line anti-tuberculosis drugs and was at 2.6%, this high proportion of resistance among previously treated cases may indicate problem with programmed performance, particularly when this resistance was among new cases is also high and subsequent surveys or periodic monitoring do not indicate a declining trend. High proportions of resistance among previously treated cases may also reflected cases reporting after treatment in the private health sector where mismanagement of cases is an issue.

Previously treated cases are a heterogeneous group, therefore differentiation by subcategory resulted in stronger analysis which led to the determination of multidrug resistance of 2.3%, as shown in table 1 and 2, the prevalence rate of mono Rifampicin drug resistance at 1.3%. These findings underscore the need for improved routine surveillance and screening of patients, through the use of better and quicker diagnostics such as the gene Xpert MTB/RIF, Line probe assay (LPA), literal flow urine lipoarabinomannan (LF-LAM) assays; TB manual (2017)[13] proactive screening of cases such as routine screening on admission of patients into medical wards of the hospital should be advocated for to ensure that cases are not missed especially in high-risk groups such as patients who failed Category 1 treatment according to Bates., *et al*. 2012 [14] and O'Grady., *et al*. 2012 [15].

Due to inadequate reporting and recording, no data were available on ranging from lab result, patient transfer, treatment out comes and HIV status as tabulated in table 3 and 6.according to. (Isaakidis., *et al*. 2013) Co treatment of DR-TB and HIV is extremely debilitating, with both medical and social impediments to adherence and so More investments should be made in improving data capturing to include data on HIV co-infection in DR-TB (Klinkenberg., *et al*. 2012) [16].

Thirdly concerning inadequate diagnostic platforms and their geographical locations for resistant tuberculosis in the district was explored such that the average distance between the health facilities in kasama district was 11.3km apart, therefore access to the gene Expert machine is an bearable, if TB was to be eradicated by 2030, this distance must be reduced in order to increase diagnostic case finding. There was no difference in the referred samples for culture at chest diseases laboratory in Lusaka as the culture results were not available. It would be important that the district plans for the Line probe assay (LPA), literal flow urine lipoarabinomannan (LF-LAM) assays; TB manual (2017) [17] platforms to assure availability of results at the shortest time possible.

The study determined the availability of the isolation facilities in the district and or the model for referral. The results showed that the district did not have any isolation facility for isolation of resis-

tant TB clients and the referral procedure was not well tabulate and some health workers were not well oriented on how best to handle the clients.

To evaluate associations between tb drug resistance and HIV status in Kasama district, it was revealed that there about three factors that were prominent as shown in tables 7 and 8. The study showed that three factors were significant and these included and not limited to patient transfers 13/305, none initiation on HAART 59/305, none compliance to drug taking or in accessible to drugs resulting in 29/305 relapse cases were seen to acerbated the problem. None documentation in the facility registers both treatment and laboratory were a sole site, therefore if we are to combat drug resistance, for the purpose of monitoring progress towards achieving national targets documentation has to be credible, although various factors promoted acquired resistance among previously treated cases, including unsupervised treatment, inadequate drug regimens, availability of ant-tuberculosis drugs without physician prescription or oversight, poor quality of the drugs supplied, weaknesses in methods for declaring patients successfully cured and substandard infection control, WHO/HTM/TB/ 2009.422 [18].

Conclusion

The study assessed the prevalence of drug resistant tuberculosis in kasama district between June 2017 and June 2018,it was found that the proportion of new TB cases that has resistance to selected first-line anti-tuberculosis at 10.7%, while the prevalence rate of primary resistance was =8.3%.and previously or (secondary) treated cases that has resistance to selected first line anti-tuberculosis drugs at 2.6%, while Rifampicin resistant at 2.3.%, by gender more men were infected than women as young adults whose age limits ranged between 22 to 30years, further there was a significant increase in the high rate of non-evaluation of treatment outcomes at 39.6%.while the cure rate drastically low at 42.56%,a situation which may need urgent attention by the district TB programmed. The comorbidity was consequently on the higher side an indication of a weak prevention and control programmed for HIV new infections.

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