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Cost Assessment of Cryogenic Preservation of Biocollections during the COVID Pandemic at CeReB 2020-2021

Aka Ayebe Kouadio Edwige ^{a*}, Diané Kouao Maxime ^a, Money Marcelle ^a, Bouagnon Rita ^a, Cissé Souleymane ^a, Kouame Kintossou Ambroise ^a, Coulibaly Litio ^a, Nguessan Felix ^a, Djaman Joseph ^{b,c} and Dosso Mireille ^d

^a Institut Pasteur of Côte d'Ivoire, 01 BP 490, Abidjan, Côte d'Ivoire. ^b Biochemical Pharmacodynamics Laboratory, College of Biosciences, Félix Houphouët Boigny University, 22 P.O. Box. 582 Abidjan 22, Côte d'Ivoire. ^c Basic and Clinical Biochemistry Laboratory, Institut Pasteur, Côte d'Ivoire. ^d Direction Institut Pasteur of Côte d'Ivoire, 01 BP 490, Abidjan, Côte d'Ivoire.

Authors' contributions

This work was carried out in collaboration among all authors. Author AAKE designed, performed the methodology and data analysis. Author DKM approved this study. The manuscript was written and edited by authors AAKE, BR, DKM, MM, CS, KKA, CL and NF compiled the collection data. All authors contributed to the article and approved the submitted version.

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ABSTRACT

Aims: Coronavirus 2019 (COVID-19) is a new human disease caused by the Coronavirus SARS-COV-2. It was classified as a pandemic by the World Health Organization (WHO) on March 11, 2020. The Institute Pasteur of Côte d'Ivoire (IPCI), through its specialized units and its Center National of Reference (CNR) for respiratory viruses, has been entrusted with the mission of coordinating the diagnostic and conservation efforts of COVID-19 for the country.

The objective of this study is to evaluate the costs of cryogenic conservation of biocollections during the COVID pandemic at the Côte d'Ivoire Biological Resource Center (CeReB) from 2020-2021.

Methodology: Cost and sample data were collected using a questionnaire administered to the

IPCI administration, the Supply Management Unit (UGA) and CeReB staff that ensured data quality.

Results: For our study period, of the 1,225,710 SARS COV 2 samples collected by National Surveillance 92.7% (1,137,210/1,225,710) were received in IPCI laboratories for diagnosis. Variable costs are higher than fixed costs in both cryovial and chaff collection production. The total production cost of the straw collection is 3.5 times the total production cost of the cryovial collection **Conclusion:** This study establishes a generic analysis of the capital and operating costs required to integrate nasopharyngeal specimen cryopreservation and can serve as a model for the implementation of cryopreservation programs.

Keywords: Straw; cryovial; costs; Biobank.

1. INTRODUCTION

Coronavirus 2019 (COVID-19) is an emerging human disease caused by the Coronavirus SARS-COV-2. It was classified as a pandemic by the World Health Organization (WHO) on March 11, 2020 [1]. This disease linked to the SARS-COV-2 Coronavirus (COVID-19) represents a significant workload for health systems [2]. In Côte d'Ivoire, the national surveillance system has counted a total of 1,225,710 suspected cases of infection requiring screening or diagnosis [3].

Studies in France, such as that of Gallien and colleagues, have analyzed the total cost of hospitalizations related to confirmed cases of COVID-19. They estimated the cost of these hospitalizations at 1.672 billion Euros, which represents an average of 7,044 Euros/stay [2]. According to Magali and colleagues, the cost of the containment and decontainment of COVID-19 in France was 31% during strict containment and 14% and 8% respectively for phase I decontainment (11 May to 31 May 2020) and phase II decontainment (1 June to 5 July 2020) [4]. Ke and Hsiao in China evaluated the cost of containment in the COVID-19 epicenter of China's Hubei Province. They find that the drastic 76-day lockdown policy of COVID-19 has had enormous negative impacts on the Hubei economy. After the government lifted the lockdown in early April, the economy recovered quickly, with the exception of the passenger transport sector, which did not rebound as quickly as the rest of the general economy [5]. In Morocco, a potential overall loss of 29.7 billion dirhams was observed after cost estimates for the first quarter of 2020 [6]. Orangi and colleagues in Kenya estimated the financial and economic costs of vaccine supply per person vaccinated with 2 doses, and the costs of vaccine delivery per person vaccinated with 2 doses [7]. The total estimated cost of COVID-19

vaccination ranges from \$348.7 million to \$436.1 million for the target population of 17.5 million in Ghana [8].

Despite all these publications, the evaluation of the costs of biopassing during the COVID-19 pandemic has not yet been studied so directly. Thus, we focused our work on the evaluation of biocollection costs during the COVID-19 pandemic at CeReB 2020-2021. The objective of this study is to estimate the economic burden of cryogenic preservation of collections by evaluating the costs of all inputs, equipment, training included in the biocollection during the pandemic of COVID-19 at CeReB.

2. METHODS

2.1 Framework of the Study

The Institute Pasteur of Côte d'Ivoire (IPCI), through one of its specialized units and Center National of Reference (CNR) for respiratory viruses, was given the task of coordinating COVID-19 diagnostic efforts for the country, with a target of 2,000 to 3,000 tests per day. Since then, this CNR of respiratory virus has used its expertise and human resources to implement standard operating procedures [9]. To ensure these operational procedures for diagnosis and conservation, the IPCI has set up a structure dedicated to the conservation, preparation and availability of biological resources (BR) of various origins. This is the IPCI Biological Resource Center (CeReB IPCI) created in 2006 and which houses the Regional Biobank of ECOWAS countries. The Institute Pasteur of Côte d'Ivoire is a public institution financed by the state and research projects.

This study to evaluate the costs of biocollection during the pandemic in COVID 19 was conducted at CeReB from April 2020 to December 2021. The biological resource center has dedicated staff. The staff complement is composed of: Six (6) research executive, Two (2) biotechnologists; Three (3) administrative officers, One (1) hygiene officer; One (1) computer specialist; Two (2) documentalists-archivists.

All the staff is civil servant, works full time and is paid by the state of Côte d'Ivoire. All the present infrastructures of CeReB have been financed up to 3, 811 million Euro (€) by the government of Côte d'Ivoire. It also ensures the fixed charge (the supply of electricity, water) and the maintenance.

2.2 COVID 19 Collection Process

The specimens collected are of three types:

 Nasopharyngeal collection specimens consisting of samples from suspected or index COVID-19 cases and or their contacts and travelers' specimens come from collection centers in Abidjan and from COVID-19 patient management centers. The serum and plasma samples from COVID-19 patients are from a project of research. The saliva collection samples are from COVID-19 positive patients, some of which were used to evaluate certain tests from automated techniques.

Two scenarios of straw cryopreservation production (manual, semi-automated) were created depending on the level of equipment used.

The manual scenario does not use any automated high-throughput equipment. The straws were filled and sealed by hand by the operators, and the straws were frozen in liquid nitrogen using a polystyrene box and a threedimensional floating platform [10]. It is possible to manually stratify 600 straws/day.

The semi-automatic scenario involves operators filling the straws using a PACE apparatus (Cryo Bio System, Saint Ouen sur Iton, France) and sealing them automatically, but they can freeze up to 3000 samples per day.

2.3 Data Collection Process

Only costs related to conservation are reported in this study.

Cost and sample data were collected using a questionnaire administered to the IPCI

administration, the Supply Management Unit (UGA) and CeReB staff that ensured data quality. The questionnaire collected information on the number of samples retained over time, capital costs and input costs. Data were also collected on the costs of storage at CeReB and cryopreservation (including preparation, equipment, small materials, consumables, office supplies, hygiene products and labor).

- Classification of costs for cryopreservation of COVID collections
- The costs were classified into 2 main groups: capital costs and operating costs.
- Capital costs included the value of resources that provide services for more than one year. These included the costs of equipment, vehicles, building space, and initial training; the costs of developing the electronic logistics management information system; and the associated cloud hosting costs. The useful life of vehicles, computers, and the electronic management system was estimated at 5 years, while the useful life of training, large equipment and machinery, and buildings were estimated at 2 years, 10 years, and 30 years, respectively. The equipment and vehicles were assumed to be used for other preservation modalities as well, and therefore their cost-effective costs were allocated based on the total number of samples and COVID-19s preserved in a year [7].
- Operating costs included resources that would need to be replaced/consumed within one year. These included costs related to consumables, preservation reagents and related supplies, personnel, transportation, all office supplies, operations and maintenance. the monitoring and supervision meetings. activities, and social mobilization activities [7].

2.4 Cost Analysis of the COVID Biocollection

The cost analysis was done by four categories of expenses. Variable costs (direct and indirect), fixed costs (direct and indirect).

Variable expenses correspond to expenses that vary with the volume of activity. These are known as operating expenses because they are linked to the volume of operations carried out within the framework of the business expenses that increase or decrease in proportion to the volume of activity.

Fixed costs (or structural costs) correspond to costs that are independent of the volume of activity. They are called structural expenses because they are attached to a production structure.

A direct cost is a cost that can be immediately added to the cost of a product, a commodity or a service, without having to make any intermediate calculations. In general, the following are considered direct expenses

- purchases of goods, raw materials and consumables
- direct labor costs (labor used directly in the production of the product or the realization of the service)

Indirect expenses require an intermediate calculation in order to be attributed to the cost of a product, a commodity or a service. This expense concerns the company as a whole [11].

The costs have been presented in euros. The average exchange rate during our study period was 1 euro (\in) = 655,957 FCFA. The data was entered into a Microsoft Excel file and then processed.

Other costs (unexpected costs during the operation) were not calculated. None of the private groups financed their initial investment with a loan. There was no method used to calculate depreciation of capital goods. For all costs, an average price was calculated, where possible, from the maximum of quotes from the equipment and materiel.

3. RESULTS

3.1 Collection Status

Côte d'Ivoire had planned to retain all samples from suspected SARS COV 2 cases, but given the scope of the pandemic on the global market and national activities, this target has been revised. For our study period, out of 1,225,710 SARS COV 2 specimens collected by the National Surveillance 92.7% (1,137,210/1,225,710) were received in the IPCI laboratories for diagnosis. These were mainly nasopharyngeal specimens.

Table 1 shows that of the samples received at the biobank for preservation, 76,116 were

collected with a preponderance of nasopharyngeal samples 65,959 samples (86.6%) followed by saliva collections of COVID 4,015 samples (5.3%).

3.2 Analysis of the Costs of the Biocollection of Straws

In Table 2, the variable costs (direct and indirect) of the collection of nasopharyngeal samples were dominated by direct variable costs at 93.3% (658,564 Euros). Among these direct variable expenses, the small direct material for the production of the straws represented 52.0% (342,147 Euro) against 48.0% in consumables (316,417 Euro).

As for the indirect variable expenses presented in Table 3 of 47112,4 Euro (6,7%) the office consumables, hygiene and liquid nitrogen represented 96,6% (45634 Euro) of these expenses.

The fixed costs of 245,342 Euro comprised 63.3% (155,495 Euro) of direct fixed costs for chaff, followed by 24.8% (60,978 Euro) of indirect fixed costs for chaff (Table 4).

3.3 Cost Analysis of the Cryovial Biocollection

Table 5 shows that the variable costs of production of the cryovial collection of 208 952 Euro were composed of direct variable costs of small material 47 042 (19,1%) and indirect variable costs in consumables and liquid nitrogen 80,1% (159 883 Euro).

In Table 6, the fixed costs (direct and indirect) of production of the cryovial collection of 162,596 Euros were composed of direct fixed costs of equipment 99,090 Euros (60.9%) and indirect fixed costs of equipment 30,489 Euros (18.8%) against an estimated labor force of 20.3% at 33,017 (20.3%).

Table 7 presents the summary and synthesis of the cost analysis of the biocollection of COVID-19 samples in straws and cryovial. It can be seen that the costs of variable expenses are higher than the cost of fixed expenses for both the cryovial and chaff collections. The total production cost of the chaff collection is 3.5 times the total production cost of the cryovial collection (1 463 345/423 964). The variable and fixed costs for the production of the straw collections are respectively 3.6 and 3.3 times higher than the costs for the cryovial production.

Collection	Number of Cryovials 2ml	Number of straw	Total n (%)
Nasopharyngeal COVID	22658	43301	65,959 (86.6%)
COVID-serum	3,181		3,181(4.2%)
COVID Plasma	2,961		2,961(3.9%)
COVID saliva		4,015	4,015 (5.3%)
Total	28800	47316	76 116

Table 1. Status of COVID-19 collections at the IPCI CRB during the study period

Table 2. Load cost analysis direct variable of the production and biocollection of 47316 COVID glitter

Designation	Amount	Costs in € (%)
Direct variable load in small equipment		
Brady	3	2,503
Welder	1	28,960
Cryogenic beaker	287	46,756
Canisters	72	263,928
Total small equipment		342,147 (52.0%)
Direct Variable Load in Consumable		
30 mm weighted rod for 0.3 ml CBS straw	47316	122,914
CBS semen straw 0.3 ml 5 x 20 straws	47316	89,259
BRADY sequin label	16743	6,815
Spangle injection nozzle	47316	97,089
Sequin suction nozzle	250	340
Total in consumables		316,417 (48.0%)
Total direct variable expenses		658,564 (93.3%)

Table 3. Analysis of variable load costs indirect from the production and biocollection of 47316COVID glitter

Designation	Amount	Costs in € (%)
Indirect variable load in small equipment		
Computer	2	1052.0
Printer	1	215.0
Micropipette	2	184.0
Bottle with wash bottle Holtex	2	12.0
Syringe 2.5cc (box of 100)	1	15.0
Total in small equipment		1478.0(3.1%)
Indirect variable load in consumables		
Tip 200 μl (1000 pieces/bag)	5	33.6
Liquid nitrogen (in liters)	10500	44820.0
ream package	1	3.7
Ink cartridge	1	12.2
Paper towels	782	509.0
hand gel	24	29.0
Autoclavable biohazard bag 10 liters	130	178.0
Latex examination gloves	40	49.0
Surgical mask	62	1,069
total in hygiene consumables		45,634.4 (96.9%)
Total Indirect Variable Charge		47112.4 (6.7%)

Designation	Amount	Cost in € (%)
Direct fixed charge in equipment		
Glitter Cryopreservers	1	99,090
PACE	1	56,405
	Total equipment	155,495(63.4%)
Indirect fixed charge in equipment		
PSM II for one seat	2	60,978 (24.8%)
Direct and indirect labor		
Biologists	3	18,523
Biotechnology technicians	1	3,040.5
computer scientist	1	4,155
Administrative	1	2,074
Hygiene officer	1	1,076
	Total labor	28,869 (11.8%)
	Total fixed charge	245 342

Table 4. Load cost analysis direct and indirect fixed production and biocollection of 47316COVID glitter

Table 5. Load cost analysis direct and indirect variable of the production and biocollection of
the 28,800 COVID cryovials

Designation	Amount	Cost in €(%)
Direct variable load Small equipment		
Cryogenic box with tube	356	9,764
Cryovials	28800	12,293
Rack	298	24,985
	Direct variable load small	47,042 (19.1%)
	equipment	
Indirect variable load in small equipment		
Computer	1	528
Printer	1	215
Micropipette	1	92
Bottle with wash bottle Holtex	1	6
	Small material indirect	841 (0.3%)
	charge	· · ·
Indirect Variable Charge in Consumable	-	
Tip 1000µl (1000 pieces/bag)	30	916.0
Label for BRADY cryovials	28800	110 147
liquid nitrogen consumable	10500	48,820
	consumable load	159,883 (80.1%
Indirect variable charge in office		•
consumables		
ream package	1	3.66
Ink cartridge	1	12.2
-	office load	15.86 (0.01%)
Indirect variable load in hygiene		
consumables		
Paper towels	782	509
hand gel	12	14
Autoclavable biohazard bag 10 liters	65	89
Latex examination gloves	20	24
Surgical mask	31	534
Hygiene load		1170 (0.5%)
Grand Total Variable Load		208,952

Designation	Amount	Costs € (%)
Direct fixed charge in equipment		
Cryoconservatives with cryovials	1	99,090 (60.9%)
Indirect Fixed Charge		
PSM II for one seat	1	30,489 (18.8%)
Direct and indirect labor		
Biologists	3	18,523
Biotechnology technicians	1	3,040
computer scientist	1	4,155
Administrative	3	6,223
Hygiene officer	1	1,076
	Total	33,017 (20.3%)
	total fixed charge	162,596

Table 6. Analysis of the costs of the indirect fixed cost of the production and biocollection of 28800 cryovials COVID

Table 7. Summary of a cost analysis of the production of the COVID biocollection from 2020 to2021 at the CeReB IPCI

Designation	Cryovial	Straw
Total quantity produced	28,800	47,316
Total variable load (CV)	208,952	705,676.4
Total Fixed Charge (CF)	162,596	245 342
Total Cost (Total Fixed Charge + Total Variable Charge)	371,548	951 018
Unit cost (CT/Product quantity) €/unit	12.9	20.1
Variable unit costs (CV/Product quantity)€/unity	7.2	14.9
Fixed unit costs (CF/Product quantity) €/unit	5.6	5.2

The unit production costs of the flake collections are twice as high as the unit production costs of the cryovials.

4. DISCUSSION

This study represents a first attempt to understand the burden of specimen storage, particularly nasopharyngeal specimens on the economics of IPCI. One of the main factors limiting the effective management of collection banks is the lack of financial resources [12].

The collection and banking of biospecimens from patients with or suspected of having COVID-19 has been essential for diagnostic testing as well as for research and development of new vaccines and drugs for the prevention and treatment of the disease [13]. Thus, the collection of COVID-19 at IPCI CeReB during the study period consisted of nasopharyngeal, serum, plasma, and saliva specimens from patients who tested positive. According to Balwir et al, blood and saliva samples from COVID-19 positive patients are essential for understanding and researching the disease when accompanied by relevant clinical data [14]. COVID-19 most commonly invades the human body through the respiratory system causing acute respiratory infections. Most guidelines and policies recommend the collection of upper or lower respiratory tract specimens for the initial diagnostic test for COVID-19 [15]. Thus upper respiratory specimens, such as nasopharyngeal and oropharyngeal swabs, are recommended for ambulatory patients and asymptomatic carriers [13].

According to the CDC, additional clinical samples of COVID-19 can also be collected from saliva, tissue, blood, feces, urine, and cerebrospinal fluid [16].

The number of cryovial samples is less than that of straws in our study. This is due to the fact that the 300 to 500 μ I straws increase the number of possibilities to be made available and the quantities produced are adapted to the needs of the current analyses avoiding waste of resources by the users (researchers). In addition, the straws occupy less space.

Regarding manual or semi-automated production of straws, it has not been able to resolve a large number of samples due to the workload associated with the production of high security straws. The fully automated scenario of high security straw production involving the use of a programmable apparatus capable of filling and sealing 3600 straws per hour is highly recommended in such a collection situation during a large-scale pandemic like COVID 19.

This study demonstrated that cryovial storage is less expensive than straw cryopreservation. The reason is that the capital costs in direct equipment and consumables were generated for the implementation of flake cryopreservation and for the items needed to achieve these different levels of automation. However, it was assumed that the biological resource center already had some standard cryopreservation equipment that did not need to be purchased for cryovial preservation (e.g., microscope, pipettes, etc.).

We estimated the cost of preservation based on the items involved in preservation. Thus, the total variable costs of samples preserved in straws are three times higher than the total costs of samples preserved in cryovials. This would mean that storage in straws uses much more inputs than storage in cryovials. The most important costs were the cost of purchasing small equipment which represented 48.5% followed by the cost of consumables which represented 44.8% of the total variable costs. Indeed, during the pandemic, laboratory activities increased due to the growing number of samples, which resulted in the use of a large number of small materials and consumables. Also, the closure of borders with the outside world had an impact on the cost of equipment and consumables. Our results are in agreement with Yahara and collaborator who showed the repercussion of the pandemic on the economy of Algeria [17].

It is also noted that the unit cost of a biocollection in straws is higher than the unit cost of a biocollection in cryovial. Unfortunately it would be advantageous to choose the storage in straws because a straw consists of 300 I of sample and a cryovial consists of 2mL of sample. For a RT PCR analysis only 140I of sample is needed. Thus with a cryovial containing the 2mL of sample we can make available for research six (6) samples put in flakes which would preserve the quality of the samples. Because the number of freeze-thaw cycles must be reduced to a minimum to avoid deterioration of the samples. This is in accordance with the instructions in the African Cancer Research Guide in which it is advised to use a small volume of aliquot to avoid freezing and thawing [18].

5. LIMITATION

Our study has some limitations, however. First, we did not include losses from samples that were tested but that we could not include in the collection and that would be in other laboratories at the institution. This underestimates the value of the collections.

Secondly, it would be interesting to conduct studies on the cost-effectiveness of conservation activities for COVID-19 samples, and other samples to make them available to the research community.

However, the costs and benefits of COVID sample collection associated with pandemic control measures involve all aspects of society, whereas our study was limited to assessing the cost-effectiveness of the collection program only from the perspective of the health sector.

In future studies, with better knowledge of longterm nitrogen sample storage, the costeffectiveness of COVID-19 sample storage with longer time horizons should be evaluated to understand the longevity of the immune response. A cost-effectiveness analysis of noncryogenic preservation interventions to estimate the financial burden of nucleic acid or lyophilized preservation intervention policies is also needed. In addition, the effectiveness of a combination of non-cryogenic crvoaenic and preservation interventions should be further studied [19].

6. IMPLICATIONS

In the years leading up to this Coronavirus pandemic, sub-Saharan Africa has been experiencing an upsurge in epidemics of emerging and re-emerging diseases such as Yellow Fever, Dengue, Rift Valley Fever, Chikungunya, Ebola, Zika virus and others since early 2000s. The strengthening the of epidemiological surveillance has led to an increase in the collection of biological resources (BR) and the requirement for their quality preservation. Due to the lack of infrastructure at the national level, a large proportion of these biological resources have been sent to industrialized countries.

Faced with this situation, IPCI has requested the State of Côte d'Ivoire to develop, since 2009, a

Biological Resources Center. This project has created an infrastructure for the conservation of biological resources from all epidemic situations, research or diagnosis, to equip them and train competent personnel to ensure their management.

As our results show, the success of the response to the disease should take into account the deployment of the program for the conservation of biological resources from infected and affected populations. Concurrent with the deployment of the response program, sample preservation interventions have made a significant contribution to local control of the epidemic and sequencing of isolated strains.

But the study also has broader implications for policy makers and researchers, as many of the world's most important biological resources (nucleic acid extracts) cannot be preserved ex situ using conventional methodologies.

7. CONCLUSION

This study establishes a generic analysis of the capital and operating costs required to integrate nasopharyngeal specimen cryopreservation and can serve as a model for the implementation of cryopreservation programs. It (the study) raised questions about the application of COVID specimen cryopreservation, as a significant percentage of biological resources were lost due to delay or lack of coordination in the collection processes of biological resources (specimens or nucleic acid extract) from COVID.

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COMPETING INTERESTS

Authors have declared that no competing interests exist.

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