

Evaluation of indicators of a neonatal screening referral service in southern Brazil during the covid-19 pandemic

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Evaluación de indicadores de un servicio de derivación de tamizaje neonatal en el sur de Brasil durante la pandemia de Covid-19.

RESUMO

Durante a pandemia por COVID-19 foi necessária uma reorganização e um novo planejamento urgente dos fluxos nos Serviços de Triagem Neonatal em todo o Brasil, com o objetivo de minimizar os impactos negativos da pandemia na atenção à saúde da população pediátrica. As principais ações desencadeadas foram a migração das coletas dos exames para as maternidades e a viabilização de consultas à distância evitando a desassistência dos casos confirmados com as doenças triadas. A partir dos novos fluxos, os indicadores de qualidade, como idade no momento da coleta, tempo de transporte das amostras, análise laboratorial e idade dos RN na primeira consulta para confirmação diagnóstica passaram por uma avaliação criteriosa. Objetivo: avaliar o impacto das medidas adotadas num serviço de triagem neonatal antes e durante a pandemia da COVID-19, no Sul do Brasil. Metodologia: estudo transversal serial de base populacional. A coleta de dados foi realizada no banco de dados do Serviço de Referência do estado do RS e na revisão de prontuários. O impacto foi estimado mediante a comparação de indicadores de atendimento do SRTN-RS a partir de setembro de 2019 a maio de 2020. Resultados: o primeiro mês de pandemia apresentou resultados com impacto negativo, mas os números foram restabelecendo-se gradativamente a patamares anteriores à pandemia, conforme novos fluxos foram sendo introduzidos no serviço. Quanto à avaliação no número de consultas, reconvocados e desfechos, foram muito semelhantes para as seis doenças triadas nos períodos pré e pós adoção das medidas de enfrentamento da pandemia, à exceção do Hipotireoidismo Congênito. Os resultados deste estudo mostraram que as rápidas ações de ajustes e adaptações tiveram impacto positivo em manter os bons indicadores de funcionamento da triagem neonatal no programa estadual durante a pandemia da COVID-19.

DESCRITORES: COVID-19, triagem neonatal, fluxos de atendimento, serviço de referência.

ABSTRACT

During the COVID-19 pandemic, an urgent reorganization and new planning of the flows in Neonatal Screening Services throughout Brazil was necessary, in order to minimize the negative impacts of the pandemic on the health care of the pediatric population. The main actions taken were the migration of exam collections to the maternity hospitals and the feasibility of remote consultations, avoiding the lack of assistance for confirmed cases with the diseases screened for. Based on the new flows, quality indicators, such as age at the time of collection, sample transport time, laboratory analysis and age of the NB at the first appointment for diagnostic confirmation, underwent a careful evaluation. Objective: to evaluate the impact of measures adopted in a neonatal screening service before and during the COVID-19 pandemic in southern Brazil. Methodology: serial cross-sectional population-based study. Data collection was carried out in the database of the Reference Service of the state of RS and in the review of medical records. The impact was estimated by comparing the SRTN-RS service indicators from September 2019 to May 2020. Results: the first month of the pandemic had results with a negative impact, but the numbers gradually returned to previous levels to the pandemic, as new flows were introduced into the service. Regarding the evaluation of the number of consultations, recalls and outcomes, they were very similar for the six diseases screened in the periods before and after the adoption of measures to fight the pandemic, with the exception of Congenital Hypothyroidism. The results of this study showed that the rapid actions of adjustments and adaptations had a positive impact on maintaining the good functioning indicators of neonatal screening in the state program during the COVID-19 pandemic.

DESCRIPTORS: COVID-19, neonatal screening, care flows, referral service.

RESUMEN

Durante la pandemia de COVID-19, fue necesaria una reorganización urgente y una nueva planificación de los flujos en los Servicios de Cribado Neonatal en todo Brasil, con el fin de minimizar los impactos negativos de la pandemia en la atención de salud de la población pediátrica. Las principales acciones realizadas fueron la migración de las colecciones de exámenes a las maternidades y la viabilidad de las consultas a distancia, evitando la falta de atención a los casos confirmados con las enfermedades cribadas. A partir de los nuevos flujos, los indicadores de calidad, como la edad en el

momento de la recolección, el tiempo de transporte de la muestra, los análisis de laboratorio y la edad del RN en la primera cita para la confirmación del diagnóstico, fueron sometidos a una cuidadosa evaluación. Objetivo: evaluar el impacto de las medidas adoptadas en un servicio de cribado neonatal antes y durante la pandemia de COVID-19 en el sur de Brasil. Metodología: estudio poblacional transversal seriado. La recogida de datos se realizó en la base de datos del Servicio de Referencia del estado de RS y en la revisión de historias clínicas. El impacto se estimó comparando los indicadores de servicio SRTN-RS de septiembre de 2019 a mayo de 2020. Resultados: el primer mes de la pandemia tuvo resultados con un impacto negativo, pero las cifras regresaron gradualmente a los niveles anteriores a la pandemia, a medida que se introdujeron nuevos flujos en el servicio. En cuanto a la evaluación del número de consultas, retiros y resultados, fueron muy similares para las seis enfermedades cribadas en los períodos antes y después de la adopción de medidas para combatir la pandemia, a excepción del Hipotiroidismo Congénito. Los resultados de este estudio mostraron que las acciones rápidas de ajustes y adaptaciones tuvieron un impacto positivo en el mantenimiento de los indicadores de buen funcionamiento del cribado neonatal en el programa estatal durante la pandemia de COVID-19.

DESCRIPTORES: COVID-19, cribado neonatal, flujos de atención, servicio de derivación.

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INTRODUCTION

The main objective of Neonatal Screening (NS) is early diagnosis in the asymptomatic phase, reducing morbidity and mortality. In Brazil, the ideal period for collecting the first sample is from 48 hours until the 5th day of the ba-

by's life, due to the specificities of the diagnosed conditions, avoiding false-positive or false-negative results. It also emphasizes the importance of managing positive cases through monitoring and monitoring of the child during the process of diagnostic confirmation and treatment. Currently, in Brazil, public screening includes six

diseases: Congenital Adrenal Hyperplasia (CAH), Biotinidase Deficiency (BD), Cystic Fibrosis (CF), Phenylketonuria (PKU), Hemoglobinopathies (HB) and Congenital Hypothyroidism (CH). 1 When not diagnosed and treated quickly, diseases can cause intellectual disability or even lead to death, directly impacting the

prognosis and quality of life of affected infants.^{1,2}

The restriction of access to health services and reduced mobility, during the global pandemic by COVID-19, affected several health policies, including neonatal screening programs. Changes in the times of collection, shipment and analysis of samples, as well as the difficulty of moving to consultations for consultations and diagnostic confirmation at the specialized outpatient clinic were some of the possible impacts expected on the services. However, despite the pandemic, care for the newborn and early diagnosis should not be discontinued, causing an increase in the number of comorbidities and diseases.

After the institution of measures to face the contingency actions, a careful evaluation of the functioning of the entire network that involves neonatal screening was necessary. The objective of the present study was to evaluate the indicators of the neonatal screening program, from the collection of the test to the diagnostic confirmation and treatment, in the periods before and after the institution of measures to combat the pandemic in the first wave of COVID-19 in Brazil, in 2020.

METHODS

This was a population-based, serial cross-sectional study carried out at the Reference Service for Neonatal Screening in the state of Rio Grande do Sul (SRTN-RS - Serviço de Referência em Triagem Neonatal do estado do Rio Grande do Sul), located at the Presidente Vargas Mother and Child Hospital (HMIPV - Hospital Materno Infantil Presidente Vargas) in the city of Porto Alegre. The Neonatal Screening Laboratory receives samples from the entire public network of the 497 municipalities in RS, corresponding to a coverage of 75% of live births in the state.⁷ The samples are mainly transported by the Post Office, through an express shipment. The study period comprised six months prior to the onset of the COVID-19 pandemic (September/19 to February/20) and during the first three months of the first wave

of the pandemic (March to May 2020). The exclusion criteria adopted were: patients older than 120 days at the first collection and samples with incomplete data, such as collection date, date of birth or birth weight. Information from the SRTN-RS database (Vega Triagem) and chart review were used. The total number of live births was obtained through a search in the Information System on Live Births (Sinasc - Sistema de Informações sobre Nascidos Vivos).⁷ The indicators analyzed were: percentage of coverage of the first collection and recollection; time for arrival of the filter paper samples at the laboratory; time for release of results; percentage of recall of new collections; mean age of newborns at the first consultation; number of diagnoses made for each of the 6 diseases screened. The recall for the collection of new samples was requested for the following reasons: sample quality, confirmation of altered results, maternal use of corticosteroids in the last fortnight of pregnancy and blood transfusion.

Quantitative variables were described as mean and standard deviation or median and interquartile range. Categorical variables were described by absolute and relative frequencies. To assess the association between categorical variables, Pearson's chi-square or Fisher's exact test and in the case of polytomous variables were used. Adjusted residuals analysis was used to locate signifi-

cant associations. To compare medians, the Mann-Whitney test was applied. The significance level adopted was 5% ($P < 0.05$) and the analyzes were performed using SPSS version 21.0.

RESULTS

From September 2019 to May 2020, 75,622 patients were analyzed in this study. As for coverage in neonatal screening, there was no significant difference before and during the pandemic ($P = 0.167$ x $P = 0.048$), in the state and municipality of Porto Alegre (Figure 1). We observed that in April there was an increase in collections in the capital, justified by the increase in collections in maternity hospitals.

Figure 2 shows the percentage of collections from 0 to 2 and from 3 to 5 days in the state and capital. From March to May, there was an increase in early collections ($P < 0.05$), compared to the months before the COVID-19 pandemic.

Table 1 demonstrates the possible impact of actions to face the contingency imposed by the pandemic on the number of recalls, the number of outcomes and the number of consultations for suspected cases. The strategies adopted did not impact the increase in the percentage of recalls during the pandemic period studied.

Among the diseases, the greatest impact

Figure 1. Percentage of coverage of NS RS and Porto Alegre in the Pre-COVID-19 (September to February) and COVID-19 (March to May) period.

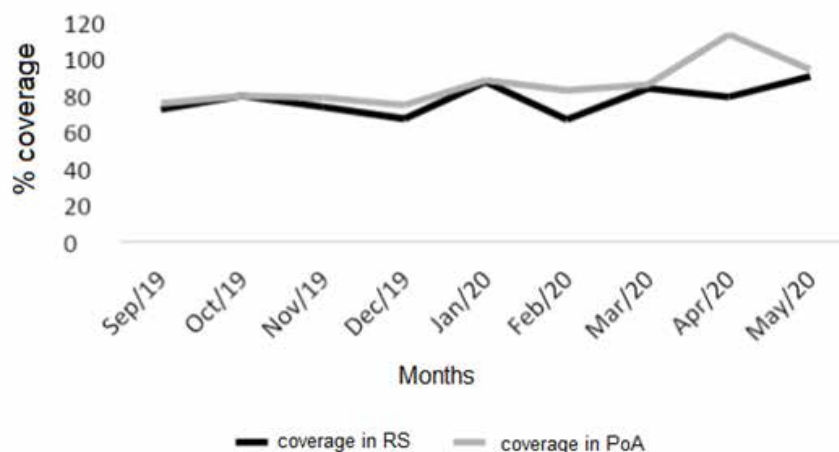
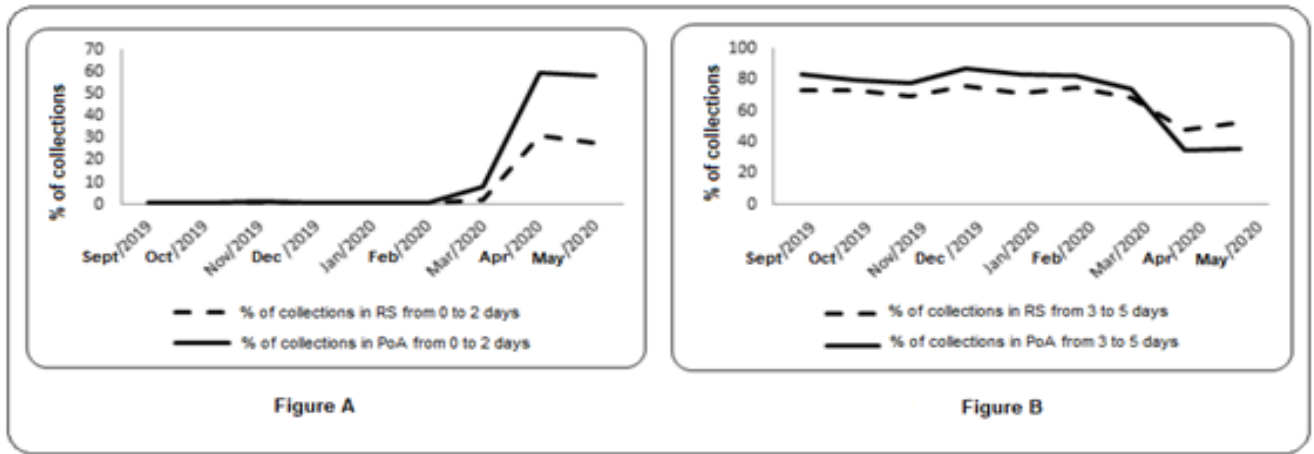


Figure 2. Figure (A) represents the percentage of the number of collections of 0-2 days of life of the NB in RS (P=0.024) and in Porto Alegre (P=0.024). Figure B represents the percentage of the number of collections at 3-5 days of life of the NB in RS (P=0.024) and in Porto Alegre (P=0.024).



was observed in HC screening. Neonatal TSH levels have different values according to age at the time of collection. Early collections led to an increase in false-positive results and the number of consultations at the beginning of the pandemic. For CAH, there was a decrease (P<0.05) in the num-

ber of consultations and recalls and an increase (P<0.05) in the number of false-positive outcomes. However, the number of patients in the pre-COVID-19 and COVID-19 phases were the same. Regarding DB, the only parameter that showed a decrease (P<0.05) was the false-positive

outcome in the COVID-19 period, thus denoting that the adjustments made did not have a negative impact on this disease. In the CF, HB and PKU screening, no statistical differences were observed in the parameters analyzed between the pre-COVID-19 and during COVID-19 period.

Table 1. Evaluation of the Pre-COVID-19 and COVID-19 periods in relation to the number of recalls, outcomes and age at the first consultation for the diseases screened by the PT.

	CAH		CH		CF		HB		PKU		BD	
	Pré COVID	COVID	Pré COVID	COVID	Pré COVID	COVID	Pré COVID	COVID	Pré COVID	COVID	Pré COVID	COVID
Recalled (P)					<0,001		<0,001		<0,001		<0,001	
Yes	7872 (14,5%)	1913 (9,0%)	1641 (3,0%)	490 (2,3%)	1708 (3,1%)	443 (2,1%)	2484 (4,6%)	754 (3,5%)	1596 (2,9%)	395 (1,9%)	2565 (4,7%)	623 (2,9%)
No	46492 (85,5%)	193,45 (91,0%)	52723 (97,0%)	20768 (97,7%)	52656 (96,9%)	20815 (97,9%)	51880 (95,4%)	20504 (96,5%)	52768 (97,1%)	20863 (98,1%)	51799 (95,3%)	20635 (97,1%)
Consultation (P)	0,02		<0,001		0,59		0,35		1,00		0,43	
Yes	47 (0,1%)	7 (0,0%)	66 (0,1%)	40 (0,2%)	33 (0,1%)	10 (0,0%)	12 (0,0%)	8 (0,0%)	5 (0,0%)	2 (0,0%)	21 (0,0%)	5 (0,0%)

No	54317 (99,9%)	21251 (100,0%)	54298 (99,9%)	21218 (99,8%)	54331 (99,9%)	21248 (100,0%)	54352 (100,0%)	21250 (100,0%)	54359 (100,0%)	21256 (100,0%)	54343 (100,0%)	21253 (100,0%)
Outcome (P)	<0,001		<0,001		0,378		0,572		0,723		<0,001	
True positive	1 (0,0%)	1 (0,0%)	43 (0,1%)	10 (0,0%)	4 (0,0%)	3 (0,0%)	8 (0,0%)	6 (0,0%)	2 (0,0%)	0 (0,0%)	4 (0,0%)	4 (0,0%)
True negative	54077* (99,5%)	20795 (97,8%)	54298* (99,9%)	21193 (99,7%)	53947 (99,2%)	53947 (99,2%)	21118 (99,3%)	54028 (99,4%)	21128 (99,4%)	54062 (99,4%)	54065 (99,5%)	21179* (99,0%)
False positive	267 (0,5%)	459* (2,2%)	14 (0,0%)	52* (0,2%)	122 (0,2%)	44 (0,2%)	3 (0,0%)	2 (0,0%)	27 (0,0%)	11 (0,1%)	256* (0,5%)	47 (0,2%)
Incomplete	19 (0,0%)	3 (0,0%)	9 (0,0%)	3 (0,0%)			325 (0,6%)	1229 (0,6%)	273 (0,5%)	98 (0,5%)	39 (0,1%)	28 (0,1%)

CAH: Congenital Adrenal Hyperplasia; CH: Congenital Hypothyroidism; CF: Cystic Fibrosis; HB: Hemoglobinopathies; PKU: Phenylketonuria; DB: Biotinidase Deficiency; P < 0.05. * Significant statistical association by residual tests adjusted to 5% significance.

DISCUSSION

NT is an important public health program. Among the various child health policies, evaluating and qualifying neonatal screening indicators during the pandemic is essential. With the imposed social distancing, the closing of numerous HUs and the reduction of professionals in primary care, there was an expectation of a reduction in NS coverage and diagnoses, which were not observed in our study. In order to minimize the negative impact of the pandemic, the services followed the guidance of the MS, authorizing collections in maternity hospitals, recommended for more than 48 hours of life of the NB.^{3,4} This orientation led to a restructuring of the SRTN flows, in order to guarantee the coverage and quality of the service, with regard to the monitoring of early collections. Similar to a study carried out in Australia, the authors emphasize that in the initial period of the pandemic, in 2020, it was necessary to devise strategies quickly, to continue the laboratory service and thus the impact on the service was not negative. This made it possible to maintain the service with no

noticeable effects on its quality, despite the challenges of quickly adapting to new work processes and working within government restrictions. The authors also highlight that the readiness and agility of implementation were based on a focus on the newborn and the family, on the production system and a mentality of continuous improvement.⁵

Our results also showed that, even with the emergency measures adopted, the autonomy of the managers of each municipality in conjunction with the nursing services, responsible for active searches and many other health programs, allowed us to advocate and maintain a global view on children's health, since there are other important programs in this context, such as vaccines, breastfeeding, childcare, which are also extremely important and needed to be maintained.^{7,8,9} Thus, in this period, municipal health strategies were instituted that prioritized home visits that met the children's and women's health programs, following up with collections at the ideal time, without impacting the coverage of the NS program.¹⁰

Due to the social distancing situation, an alternative was to leverage the tele-service modality. It was recently regulated by

the Ministry of Health, the Federal Council of Medicine and the Federal Council of Psychology. Guidance in this regard has been published by the International Red Cross and the Center for Studies and Research in Health Emergencies and Disasters.^{11,12,13,14} This alternative allowed agility in the contact with health teams of the municipalities for suspected cases and quick measures to confirm diagnoses and institute treatments. Schwamm (2014) emphasizes that telehealth is the provision of health services mediated by technology. It can be strategically seen as a disruptive innovation that puts traditional health practices in check, with cost reductions and gains in quality, access and user satisfaction.¹⁵ Corroborating this, it is worth highlighting, then, Ordinance 467 of the Ministry of Health, which authorizes the practice of telemedicine, to serve patients in the midst of the current pandemic, from a distance.¹¹ From this perspective, Greenhalgh comments that online service modalities have been prioritized and widespread, which imposes the need to quickly extend access to cell phones and the Internet to professionals and users. The remote consultation must be carried out based on

protocols, with clear and objective messages, giving preference to video.¹⁶ Thus, it is possible to provide quality care at a distance, guiding and training local health teams, avoiding unnecessary displacements and minimizing the chances of exposure to the virus, in the current context. In this way, tele-consultation proves to be a very effective coping action, which can also contribute to the monitoring of most of the population, avoiding the agglomeration of hospital fields where there is a high risk of contagion.¹⁶

Each of the six diseases screened has a peculiar clinical picture and specificities for screening, which requires individualized flows and perspectives.¹ For the diagnosis of PKU, early collections can significantly impact the outcome, since phenylalanine is generated by the metabolism of proteins ingested after birth. If the collection is performed before this process, false-negative results may occur.^{1,17,18,19} Although early collections present a risk for the diagnosis of PKU, no statistical differences were observed in the two periods evaluated in terms of consultations, outcomes and percentage of recalls. In the same way, even with the increase in the transport time of the samples, there was no impact on the parameters analyzed for DB, since the activity of biotinidase decreases significantly with the action of high temperatures and humidity.²⁰ In the case of CAH, early diagnosis is crucial to prevent infant death from adrenal insufficiency. Screening programs for CAH are mainly aimed at early diagnosis of the most severe and potentially lethal salt-wasting form.^{6,21} Despite the decrease in the number of consultations for HAC during the pandemic, the number of patients in the pre-COVID-19 and COVID-19 phases was similar. This result is attributed to the agility of the team in seeking clinical information and results of collections of suspected babies and in this way quickly concluding on the outcome and guiding the local teams.

Regarding the HC, the collection in the maternity hospitals had an impact on the number of consultations and the percentage of false positives. The values of the TSH

hormone are higher in the first 48 hours of

Each of the six diseases screened has a peculiar clinical picture and specificities for screening, which requires individualized flows and perspectives. 1 For the diagnosis of PKU, early collections can significantly impact the outcome, since phenylalanine is generated by the metabolism of proteins ingested after birth. If the collection is performed before this process, false-negative results may occur

the newborn's life.^{22,23,24,25} With the increase in early collections, the number of falsely high results generated a greater number of consultations, until the service established new reference values for this test in the period from 0 to 48 hours of the NB's life. There was no influence on the number of recalls, as the initial strategy was to refer suspected patients directly to the consultation without collections, in order to speed up the diagnosis process, since CH requires the beginning of treatment until the 15th day of the baby's life to avoid neurological sequelae.^{22,23,24,25}

Despite the contingency imposed by the pandemic, there was the active participation of the Municipal Health Departments (SMS - Secretarias Municipais de Saúde), maintaining the flows and programs aimed at the integral health of children. Measures were adopted that effectively contributed to the achievement of the program's purposes, including household collections, reinforcing the need for collaborative networks and all that, with the joint work of the nursing team and the entire multidisciplinary team.

The contingency measures significantly affected transport flows, with the closing of post offices, restrictions on intercity mobility and reduction of health teams, the means of transferring samples from NS were hampered. After the most delicate and initial moment of the pandemic, a progressive resumption was observed in the normal flows of service at the HUs and in the state and municipal transport systems. In this perspective, Aquino et al reinforce that the reorganization of Primary Health Care (PHC) services to simultaneously face the epidemic and maintain the regular offer of its actions is imperative.²⁶ The routine activities of the PHC also need to be preserved in times of a pandemic, especially if we consider that the forecasts point to a long course of living with the new virus, with alternation of greater and lesser social isolation, which requires readjustment of certain procedures, including new forms of daily care at a distance, avoiding the risk of deepening the exclusion of access and social inequalities.²⁷

CONCLUSION

The initial period of the COVID-19 pandemic generated many restrictive actions that could significantly impact the proper functioning of the SRTN. But with the present study, it was observed that, with

the rapid reorganization of the network and changes in flows, there was not a major impact on the Service. In addition, the implementation of telemedicine has strengthened relations with the primary care medical teams of the municipalities for the discussion of suspected cases and those in the diagnostic phase with the aim of

qualifying them for the initial care of these babies. The Service will continue to evaluate, until the end of the pandemic, possible changes in the quality indicators, so that, if necessary, quick and efficient measures are taken, avoiding any negative impact on the diagnosis and care of NS.

ETHICS APPROVAL:

The project was approved by the Research Ethics Committees (CEP - Comitês de Ética e Pesquisa) CAAE: 32217520.8.0000.5345 and from the HMIPV CAAE: 32217520.8.3001.5329, from the Federal University of Health Sciences of Porto Alegre (UFCSPA).

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