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Structure, Process and Outcome Evaluation of Central Public Health Laboratory Performance About Neonatal Screening Program in Karbala in 2022

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***Abstract*-Background: Neonatal screening is a preventive medical act aims to early detecting neonates affected by specific disorders that endanger their lives or cause long-term health problems and require prompt intervention. This can result in significant reductions in morbidity, death, and related costs and disabilities. The panel of neonatal screened disorders has been gradually expanded. Expansion has been empowered with the introduction of tandem mass spectrometry, which allowed for the screening of up to 40–50 diseases with a single blood spot. Part of the implementation of neonatal screening program must include, just like any other program, monitoring and evaluation task in order to identify difficulties or barriers to improve procedures and methodologies. This study aimed to evaluate the Central Public Health Laboratory/ Karbala Directorate of Health performance in Neonatal Screening program. Method: The evaluation method has been carried out in Holy Karbala Governorate for the period between the first of September 2021 and the end of June 2022 using a check list of standards taken from the National Guideline for Newborn Screening for Care Providers in Primary Health Care Centers in Iraq. This was to evaluateCentral Public Health Laboratory by meeting the manager employee and evaluate theCentral Public Health Laboratory room. Results: The Central Public Health Laboratory showed an acceptable level of implementation. However, from the structure point of view, there were some difficulties in maintaining sustainability of providing some vital material resources like test kits. From the process point of view, there have been difficulties in the transmission of blood samples to the laboratory, which happened only two days a week.Conclusions: Since the program's importance in detecting diseased cases early and can save infant lives, it is critical to organize work in the program and maintain the availability and continuity of laboratory materials required for the continuation of work. Recommendations: The research was conducted during the program's stop due to the lack of laboratory supplies, thus it is recommended to re-evaluate the same organization at a period when work is active.**

***Keywords*-neonatal screening, congenital metabolic disorders, rare diseases, dried blood spot screening.**

I. INTRODUCTION

Neonatal (newborn) screening was began in Europe in the 1960s when small programs to screen congenital phenylketonuria had been conducted (Woolf and Adams, 2020). After which, many countries started neonatal screening programs more than 40 years ago to identify newborns with abnormalities that, if detected and treated early, might prevent severe irreversible health damage. Phenylketonuria was the first disorder for which newborn screening programs were established in many countries (Knapkova*et al*., 2018). Then screening for the disorders, hypothyroidism and galactosemia, has quickly achieved widespread acceptance in newborn screening programs (Raffle and Gray, 2019). Over the following few decades, the programs were gradually expanded. Even some congenital rare diseases with major impact on people have been included. Screening techniques like tandem mass spectrometry, as well as more treatment options, have led to the development of screening programs in several countries since the turn of the century (Cornel*et al*., 2014). Thousands of children with genetic and metabolic disorders have had the chance to live a healthier life as a result of such an early detection and treatment (McKusick, 2007).According to the Iraqi national guideline, all babies are offered screening for phenylketonuria, congenital hypothyroidism, and galactosemia.

Phenylketonuria is a rare metabolic disorder characterized by insufficient phenylalanine to tyrosine conversion. The buildup of extra blood phenylalanine, if left untreated, can cause neurological, physiological, and intellectual problems (Brown and Lichter-Konecki, 2016).

Classic galactosemia is the loss of galactose-1-phosphate uridylyltransferase activity, while Duarte galactosemia, the more common clinical variation, is caused by partial enzymatic impairment (Elsas*et al*., 1995 and Berry, 2021). Galactose-1-phosphate uridylyltransferase effects lead to galactose buildup, galactitol formation, and faulty galactosylation and glycosylation (9). If this metabolic disorder goes undiscovered and untreated, it causes

increasing morbidities that impair and threaten quality of life. Jaundice, liver failure, and sepsis are possibilities, as are mild neurologic complication and motor derangements to severe handicapping, renal tubular malfunction, cataracts, ovarian dysfunction, and mortality (Connor, Elle Davies et al., 2015) (11) (Colditz and Colditz, 2010).

The deficiency of thyroid hormone at birth is referred to as congenital hypothyroidism. Thyroid hormone deficiency is most commonly caused by the problem with thyroid gland development (dysgenesis) or an abnormality in thyroid hormone production at birth (dyshormonogenesis) (Rastogi and LaFranchi, 2010) cited in (Bowden and Goldis, 2020). Congenital hypothyroidism has been related to an increased risk of birth defects (Olivieri*et al*., 2002) cited in (Veisani*et al*., 2014). Thyroid diseases, both hypothyroidism and hyperthyroidism, have a serious effects on muscles, as progressive muscle damage leads to an increase in creatine kinase(Klein*et al*., 2017)cited in (Najim*et al*., 2020). Hypothyroidism can affect female fertility in a variety of ways, including hormonal effects (Liu*et al*., 2018) cited in (Amer*et al*., 2020).

Thousands of infants with genetic and metabolic disorders have had the opportunity to improve their lives as a result of early detection and treatment. Unfortunately, many countries' screening programs were unable to expand beyond a few diseases. The absence of screened diseases in these countries is due to the lack of structured screening organizations as well as financial limitations (Shorter*et al*., 2011).

The concentration and/or the activity of metabolites and/or enzymes may be used in screening tests. If the result exceeds the expected range, it is considered test-positive. The level set strikes a balance between sensitivity and specificity. An extremely high specificity cut off may result in false negatives. A test with high sensitivity cut-off may result in a large number of false positives (Cornel*et al*., 2014).

Screening methods in Iraq

Newborn screening is a complex system that can be distributed into 3 stages (22). Nationally, these have been implemented according to the National Guideline for Newborn Screening for Care Providers in Primary Health Care Centers in Iraq:

1. Pre-analytical (education and specimen collection): In primary health care centers, every newborn aged 3-5 days (the optimal age after birth), which extends to 1 month of age, is tested via the screening program simultaneously with getting the BacilleCalmette-Guérin vaccine. The healthcare experts explain the screening test and its worth to newborns, as well as encourage parents, especially mothers, to participate in the program. Blood specimens are collected and delivered each two days to the Central Public Health Laboratory.
2. Analytical at the Central Public Health Laboratory: According to the Guidelines, the outcome of newborn screening could be one of two:
    a. Negative results.
    b. Positive results: this does not indicate that the infant has the disease, but s/he is thought to be at greater risk of being diseased.
    c. Confirmative result: confirmatory tests should be conducted to prove congenital hypothyroidism using sample filter paper, whereas phenylketonuria and galactosemia are confirmed using new filter paper.
3. Post-analytical (follow-up, education, management, and evaluation) in Baghdad, at either the Central Child Teaching Hospital or the Al-Imamain Al-Kadhimin Teaching Hospital screening clinics, pediatricians will monitor and manage the sick child's health. (23).

II.METHOD

Between the first of September 2021 and the end of June 2022, this evaluation study was carried out. It was conducted in the Holy Karbala Governorate. This governorate is located approximately 105 kilometers southwest of Baghdad the capital of Iraq.It has an area of approximately 52,856 km^2 and a population of 1,350,577 in 2022 according to the data ofcentral statistical organization Iraq.

This study is a trial to assessthe pilot program administered by the Governorate Directorate of Health in the Central Public Health Laboratory. Accordingly, the data was gathered from the Department of Public Health via a check list. After reviewing the National Guideline of Newborn Screening for Care Providers in Primary Health Care Centers in Iraq and literature, the list was structured and examined for validity and reliability. The evaluation of the Laboratory performance was divided into three approaches:

1. Structure approach
2. Procedure approach
3. Outcome approach

Structure approach: This section of the evaluation check list assessed the program's human and material resources for blood sample analysis including the availability of trained laboratory workers, laboratory room, DELFIA Time-Resolved Fluorescence devices, pipettes (10ml), pipette rubber, glass bottle (250ml), multichannel pipit 12*200 (4 pieces), tips 200, trough (4 pieces), Galactose level test kit, neonatal Phenylalanine level test kit, neonatal hypothyroidism test kit, and neonatal hypothyroidism test kit, refrigerator, records and procedure guidelines.

The process approach was conducted by visiting and interviewing the relevant health staff who were in charge of the program. Because of data collection in the program had stopped at the time of the interviews, the process of evaluation based only on questioning the participants, not directly observing the process. The approach used the check list to assess the number of daily work hours and days of work per week, number of training courses, and time between blood sample receipt and analysis.

Outcome approach: This section of the check list investigated the number of patients diagnosed and followed up on by the laboratory.

III. Results

A. *Outcome approach:*

During eight years in the program, about 204,816 tests were carried out. Figure 1 shows that 63% of patient diagnosed in the CPHL in patients age less than one month in the diagnosis date and live in Holy Karbala Governorate.

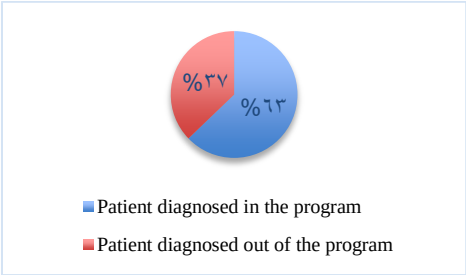

Figure1: Percent of patient diagnosed in the program according to the including in the research

Table 1 shows that the most common disease subset in the first screening test was congenital hypothyroidism, with 390 positive tests, and 192 infants had positive confirmatory tests among the 245 children diagnosed in the program. according to the table, only 29 cases were followed up at the central public health laboratory, and nearly all of them had phenylketonuria.

Table 1: outcome approach of the central public health laboratory shown as number of identified patients

S.	Disease	Diagnosed	Followed up
1	Galactosemia	18	1
2	Phenylketonuria	35	28
3	Congenital hypothyroidism	192	0
Total		245	29

B. *Structure approach:*

Table 2 displays that there are a number of laboratory tools available. However, there are no guidelines for the type or quantity of instruments required.

Table2: Structure approach of the Central public Health Laboratory*

s.	Item	Standard	Availability**	Sustainability
1	Trained laboratory staff	……	4	4
2	Lab room	……	2	2
3	DELFIA Time-Resolved Fluorescence devices	……	1	1
4	Tibs 1000µ	……	2	2
5	Automatic pipette 1 ml	……	3	3
6	Stop watch (2pcs)	……	4	4
7	Pipette 10 ml	……	5	5
8	Pipette rubber	……	4	4
9	Multichannel pipette 12* 200µ (4pcs)	……	10	10
10	Tips 200µ	……	25000	25000
11	Bottle glass 250 ml	……	3	3
12	Trough (4pcs)	……	6	6
13	Neonatal TSH test kit	……	Depends according to the contract between the Iraqi Ministry of Health and the supplier company	Same as Availability
14	Galactose Level test (galactosemia) kit	……	Depends according to the contract between the Iraqi Ministry of Health and the supplier company	Same as availability
15	Neonatal Phenylalanine Level test (PKU) kit	……	Depends according to the contract between the Iraqi Ministry of Health and the supplier company	Same as availability
16	Refrigerator	……	1	1
17	Records	……	3 types	3 types
18	Procedure guideline	……	1	1

* The standard structure relevant to the program for the central laboratory is not found in the National Guideline of Newborn Screening for Care Providers in primary health care centers in Iraq.
** The numbers in the availability field indicate the number of the item.

C. Process approach:

Table 3 shows that work on a sample begins right away. Work was performed four days per week.

Table 3: Process approach of the central public health laboratory

S.	Item	Standard *	Availability No. (%)	Sustainability No. (%)
1	Number of working hours per day	6	6 (100)	6 (100)
2	Number of working days per week	4	4 (100)	4 (100)
3	Number of training courses	Not mentioned	12(….)	……
4	Time between blood sample receipt and analyzing	1 day	1 day (100)	1 day (100)

* The samples were transferred twice weekly to the Central Public Health Laboratory, according to Iraqi Ministry of Health guidelines, so that they could be evaluated four days a week. This strategy was not included in Iraq's National Guidelines for Care Providers in Primary Health Care Centers.

IV. Discussion

A. Outcome evaluation

In the Central Public Health Laboratory, where the total number of screening tests performed was 21342. The results showed that 0.0899% of people who screened displayed a positive diagnostic test for congenital hypothyroidism, while according to Iraq's National Guidelines for Care Providers in Primary Health Care Centers, the birth incidence of congenital hypothyroidism was about 1:3,000 newborns in the Caucasian population. In Iran, the incidence was 2/1000, whereas in Turkey prior to the program, the incidence was (1/2736-1/2326) (26, 27). These differences in the incidence may be because of different TSH cutoff values and may possibly due to the regional differences in the levels of iodine deficiency (Taj-Aldeen*et al*., 2019).

Moreover, the results illustrated that about 0.008% of screened infants were diagnosed as having galactosemia, while the birth incidence of classic galactosemia is about 1 per 50,000–60,000 in the Caucasian population according to the national guideline of Iraq. The occurrence of galactosemia in southern Iran was 1:6000. On the other hand, the incidence of galactosemia in the countries which implement screening programs on galactosemia is variable; for example, among white Americans it is around one patient in 47000. In the United Kingdom, the ratio was one patient in 70000, and in Ireland, one patient in 23000 (Hettiarachchi and Amarasena, 2014).

Regarding phenylketonuria, the results demonstrated that about 0.016% of those screened had positive results, while the incidence of the disorder is 1:10000, according to the National Guideline of Newborn Screening for Care Providers in primary health care centers in Iraq. This ratio varies in different countries; in Iran the incidence was 1:6662 in live births. The highest incidence was found in Arabian countries (more than 1:5000) and Turkey (1:2600). The reasons behind these differences might be hereditary, population awareness, consanguinity marriages, and the difference in the coverage rate of screening (Rose*et al*., 2006).

In the period of collecting information, it was found that a number of children had been followed up on by the Central Public Health Laboratory due to the availability of testing materials and their unavailability in hospitals. As a result, rather than screening, laboratory resources have been used for follow-up. The number of children with congenital hypothyroidism, phenylketonuria, and galactosemia who had regular follow-up at the Central Public Health Laboratory was 0, 28, (80%), and 1, (5.5%), respectively. The patients had to be followed up on at the hospital, which includes a team of trained specialized physicians, a laboratory, medicines, and nutritional services.

B. Structure evaluation

One of the most important requirements for the program's continuation at the Central Public Health Laboratory is the continuous availability of laboratory materials. However, the need for these supplies was not determined precisely in the current study because this information is not available in the national guideline of Iraq.

The availability and continuity of the congenital hypothyroidism, Galactose Level, and Phenylalanine Level test kits. The availability of these materials was one of the tasks of the company contracted with the Iraqi Ministry of Health.

More than one temporary suspension occurred in the program owing to the delay in the provision of laboratory materials by the company. And that's due to a variety of factors, including the epidemic of COVID-19. The last pause was from September until the time of this research. The program's stopping dates are shown as below:

1. From 7/11/2016 to 13/2/2017
2. From 26/7/2017 to 25/9/2017
3. From 6/5/2019 to 19/11/2019
4. From 20/9/2021and until the time of conducting the current evaluation study.

C. Process evaluation

One of the most important goals of the program is the early detection of the targeted diseases in order to early treat patients and preserve their safety. However, in the governorate of Holy Karbala, samples were received on only two days a week, and Central Public Health Laboratory analyses have been done to make the initial suspect case and contact the parents to take the confirmatory sample. According to the Guide for Newborn Care Providers in Ontario, it is critical that the newborn screening organization obtain the newborn screening cards once possible after collecting the blood. Thus, the cards are sent no later than one day after

collection and, perfectly, as soon as the blood spots on the card are dry (at least 3 hours after collection). Newborn with one of the diseases screened can start to developed ill and may suffer irreversible damage soon after birth (Ontario, 2015).

The training of all laboratory staff who engaged in the program in health centers was among the Central Public Health Laboratory responsibilities.. This aims toincrease the knowledge of employees in these centers. Unfortenatually, such trainingswere not carried out.

V.CONCLUSION

Because of the importance of the program in detecting diseased cases early and protecting infants lives, as well as discovering a number of cases in the governorate, in the Central Public Health Laboratory, organizing work in the program and maintaining the availability and continuity of laboratory materials was done .the high incidence rate of diseases that screened was observed.

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