

Modification of infant hypothyroidism and phenylketonuria screening program using electronic tools

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ABSTRACT

Background: Congenital hypothyroidism and phenylketonuria (PKU) are the most common cause for preventable mental retardation in infants worldwide. Timely diagnosis and treatment of these disorders can have lasting effects on the mental development of newborns. However, there are several problems at different stages of screening programs that along with imposing heavy costs can reduce the precision of the screening, increasing the chance of undiagnosed cases which in turn can have damaging consequences for the society. Therefore, given these problems and the importance of information systems in facilitating the management and improving the quality of health care the aim of this study was to improve the screening process of hypothyroidism and PKU in infants with the help of electronic resources. **Methods:** The current study is a qualitative, action research designed to improve the quality of screening, services, performance, implementation effectiveness, and management of hypothyroidism and PKU screening program in Isfahan province. To this end, web-based software was designed. Programming was carried out using Delphi.net software and used SQL Server 2008 for database management. **Findings:** Given the weaknesses, problems, and limitations of hypothyroidism and PKU screening program, and the importance of these diseases in a national scale, this study resulted in design of hypothyroidism and PKU screening software for infants in Isfahan province. The inputs and outputs of the software were designed in three levels including Health Care Centers in charge of the screening program, provincial reference lab, and health and treatment network of Isfahan province. Immediate registration of sample data at the time and location of sampling, providing the provincial reference Laboratory and Health Centers of different eparchies with the ability to instantly observe, monitor, and follow-up on the samples at any moment, online verification of samples by reference lab, creating a daily schedule for reference lab, and receiving of the results from analysis equipment; and entering the results into the database without the need for user input are among the features of this software. **Conclusion:** The implementation of hypothyroidism screening software led to an increase in the quality and efficiency of the screening program; minimized the risk of human error in the process and solved many of the previous limitations of the screening program which were the main goals for implementation of this software. The implementation of this software also resulted in improvement in precision and quality of services provided for these two diseases

and better accuracy and precision for data inputs by providing the possibility of entering the sample data at the place and time of sampling which then resulted in the possibility

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of management based on precise data and also helped develop a comprehensive database and improved the satisfaction of service recipients.

Key words: Hypothyroidism, infants, phenylketonuria, process digitalization, screening

INTRODUCTION

Congenital hypothyroidism or CH is among the most common causes of preventable mental retardation worldwide.^[1] The hypothalamic-pituitary-thyroid axis starts functioning during mid-fetal life, and this activity continues till birth. If hypothyroidism is present in the embryo, it can lead to abnormalities in important organs such as central nervous system and skeleton. However, most infants with this disorder look completely healthy at birth. Therefore, given the effect of thyroid hormone on brain development, small and nonspecific symptoms of hypothyroidism in infants, and irreversible effects of this disorder, for many years hypothyroidism screening has been carried out in various countries.^[1] This screening first started in North America in 1972 and later spread to other countries.^[2,3] The prevalence of this disorder in United States is 1/400 infants.^[4] In Iran, the CH prevalence is 1/914 in Tehran,^[5] 1/303 in Kashan,^[6] and 1/338 in Isfahan^[7] which shows a relatively high prevalence for CH in Iran. Phenylketonuria (PKU) is another rare congenital metabolic disorder. The main cause of this disorder is an accumulation of phenylalanine in bodily and neurological fluids. This accumulation is due to lack of the necessary enzyme for the metabolism of phenylalanine to tyrosine. The unnatural accumulation of this amino acid in infants' bodies are dangerous and can lead to disorders in the skin and nervous system.

Reviewing the adverse effects caused by this disorder and heavy cost of health care for the infants suffering from them shows the necessity of adopting policies for prevention, treatment, and control of this congenital disorder^[8-10] and can also provide important epidemiology and pathophysiology information about the society.^[11]

Currently, most developed countries around the world carry out systematic screening programs for screening of hypothyroidism in infants. In Iran, this screening program has been implemented in various provinces including Isfahan province since year 2004 (2003) but the current program has several problems and limitations that necessitate changes in the screening process. These problems include:

- Lack of control and monitoring on the sampling process which can lead to loss of the suitable time period for sampling in case of re-sampling
- Lack of proper control and monitoring on all the samples gathered from various health centers in the central reference lab due to lack of a comprehensive daily list of all the samples
- Inability to monitor the time between sampling and testing of samples in the lab

- Inconsistencies between number of damaged samples reported by health centers and number of samples reported by the lab
- Several problems in the information recorded in quarterly report forms and uncertainty in the recorded information
- Inconsistency in the post bill due to inconsistency in the number of samples reported from each health center (10–20 million Rials each month)
- Risk of lost samples during transit between sampling centers and reference lab due to reference lab being unawareness of the number of samples, sampling location, and other important information
- Loss of time and possibility of human error due to manual recording of information
- Lack of the proper answer to the family of infants given the fact that the family pays the cost of tests.

Therefore, given these problems this study aims to use electronic tools in order to improve the quality of hypothyroidism and PKU screening program, the effectiveness of management of the hypothyroidism and PKU screening program and the quality of different stages of screening and also reduce the possibility of human error, reduce the cost of the program and finally reduce the prevalence of hypothyroidism and PKU.

METHODS

This study is a qualitative, action research designed to improve the quality of screening, services, performance, implementation effectiveness, and management of hypothyroidism and PKU screening program in Isfahan province. In order to design the appropriate software, all constraints, problems and challenges in hypothyroidism screening program were evaluated. The opinions of experts and end-users were also consulted. After gathering a comprehensive list of the problems and challenges of hypothyroidism and PKU screening program and gathering the opinions of experts and end-users in different levels of health services including Health Care Centers, health and treatment networks, province Deputy of Health and Provincial Center of Health, in order to create the necessary scenario for design and creation of software the project was divided into the following phases:

1. Identifying and documentation of the process of hypothyroidism and PKU screening program at different levels: In this stage all stages of screening program carried out by different health care providers including health centers, central health care facilities of eparchies, Provincial Center of Health and the provincial reference laboratory were identified and documented
2. Identifying the connections: In this stage the relationships between different processes and people (including health provider, technicians, experts of eparchy health center,

- Province Laboratory Technicians and Center of Disease Management) were identified
3. Investigating the information exchange between different processes
 4. Interviewing people: In this stage related individuals at different levels were interviewed, and problems and challenges in information transfer processes, information forms and notification of families were identified
 5. Identification of needs: In this stage the needs and expectations of end-user from a digitalized information system were identified
 6. Development of software design patterns
 7. Coding of the final software and receiving feedback from experts regarding different stages of software design
 8. Making corrections during software design based on the feedback from experts and end-users
 9. Experimental implementation: In this stage, in order to identify the technical problems, the software was implemented at a pilot project in four different eparchies
 10. Full implementation of the software in Isfahan province.

The details of the screening process for infants is as follows:

In this screening program, all born infants must undergo the screening test no later than 4 days after birth. This program has been implemented in Isfahan province since year 2003 (1382). The family of the infant must take the newborn to the nearest health center or clinic where the heel sample of the infant is taken using specialized filters. The technician in charge of sampling fills a form titled "form number 1 for infant screening program" and attached the sample to the form.

This software creates the possibility of alerting the sampling technician, labs in charge of experiments and management and supervision positions (in different Eparchies or Province Center).

The programming was carried out using Delphi.net software and SQL Server 2008 was used as database management program. The information transfer between servers was carried out in real-time.

Findings

By identifying the weaknesses, challenges, problems, and limitations of hypothyroidism and PKU screening program, and given the importance of quick diagnosis of these disorders and the costs of treatment, this study resulted in creation of software for careening of hypothyroidism and PKU in infants. The details of the software are as follows:

The user interface of the software includes three levels:

- Level 1: Entering the information of form number 1 of the screening, which is carried out in sampling locations (Local Health Centers or Clinics) and by the sampling technician. Fixing the screening information based on the request by provincial reference lab, follow-up on damaged or incomplete samples and re-sampling and delivery of the written test results to the infants' families are also carried out in this level

- Level 2: Eparchy's Center of Health which is in charge of supervising the sampling process and follow-up on damaged samples and re-samplings
- Level 3: Provincial reference lab under provincial deputy of health which is in charge of accepting samples, confirming the integrity of samples (comparing the information received from software with information attached to the sample and sending the confirmation to the lab in order to start the tests), creating daily schedules using the software, management of the quality of the samples and test results in an online manner with the help of the software, recording the test results in software database and evaluation of the test results by the manager of reference lab and adding the digital signature to the test results.

Another part of the software is the outputs, which are also organized in three levels:

1. At the level of health centers carrying out the screening program, the outputs include:
 - List of samples based on the date of sampling, which is printed at the end of each day and sent to reference lab with samples themselves
 - List of samples with a final confirmation, which indicate nominal samples and normal results
 - The test sample of each infant based on the family name or national ID code of the mother, follow-up code or filter number. If an infant required more than one test, a linear list of all tests is displayed, and it is possible to receive the report of a specific filter number for that infant
 - List of recalled samples during a time period specified by the user
 - List of damaged samples during a time period specified by the user
 - List of thyroid stimulating hormone (TSH) and PKU recalled samples during a time period specified by the user.
2. Provincial reference lab:
 - Daily schedule based on the number of received samples
 - List of samples tested each day (an 86 item list for each lab technician based on the number of test kits available to each technician)
 - Test results based on daily schedule
 - List of samples with a final confirmation, which indicate nominal samples and normal results for the entire province
 - The test sample of each infant based on the family name or national ID code of the mother, follow-up code or filter number. If an infant required more than one test, a linear list of all tests is displayed, and it is possible to receive the report of a specific filter number for that infant
 - List of recalled samples for the entire province during a time period specified by the user
 - List of damaged samples for the entire province during a time period specified by the user

- List of TSH and PKU recalled samples for the entire province during a time period specified by the user.
3. At the level of provincial health care networks:
- The statistics of samples taken by each health center during a time period specified by the user
 - The number of unsuitable samples taken by each health center and the total number of unsuitable samples in each eparchy
 - List of recalled samples for each center, eparchy, and total
 - Statistical reports of TSH and PKU test results for each health center and eparchy
 - The statistical reports of samples submitted by each center participating in the screening program.

Currently and with the implementation of the screening software, the sampling technician immediately enters the sample information into the software and provides the family of the infant with a tracking code used in future follow-ups and for receiving the test results. Since the information transfer is carried out in online format, the technicians in provincial reference lab know the number of the samples taken and are informed about the number of samples received the next day, the source of the samples and other related information. Before the implementation of the software, the provincial reference lab had no data regarding the number of samples taken each day, and given the fact that the samples are transferred using post, it was possible for a number of samples to get lost during transfer without reference lab noticing and each eparchy receiving only reports regarding samples with positive TSH. This led to the possibility of samples that got lost in the transfer and did not undergo the test belonging to an infant with positive TSH. This lack of result would lead to adverse effects on the infant. This software is designed in a way that before entered the lab, the quality and information of the received samples are carried out by sample admission and only confirmed samples are transferred to the lab. If a sample is missing, it will be discovered due to disconformity between the received samples and sample data provided by the software and the software immediately alerts the sampling technician. Then the re-sampling will be carried out without delay. The same process applies to samples that lack the proper quality for testing, and if sample's quality is below optimum, the software alerts the sampling technician to carry out re-sampling. The software also alerts the manager of the health center about the missing or unsuitable samples so that the manager can follow-up on re-sampling requests in case the sampling technician does not pay attention to the alerts.

After comparing the list of samples with received samples and confirming samples, the software transfers the information of the samples to the lab and creates a daily work schedule for the lab. This process was previously carried out manually by the lab technicians, which was a time-consuming process with a large possibility for mistakes. Currently, the software creates a work schedule for each technician based on the number of accepted samples and technicians follow the list and test the samples one by one. If the result of the test

for one of the samples is unsatisfactory, the samples are transferred to the retesting list. This list is also created by the software. The testing apparatus directly transfers the results to the software, removing human involvement, thus saving time and resources and reducing the possibility of error to 0%. Since it is necessary to provide the family of the infants with detailed and official test results, the chief technician of the reference lab reviews each test result and verifies them with an electronic signature. After receiving the electronic signature, the results are instantly available to the provincial manager of the program, the chief technician of each eparchy and the sampling technician. Afterward, the sampling technician or any other person with suitable security clearance can print out the results and send them to the families of the infants. There is also the possibility of informing the family of the infants using SMS services and families can also view the test results using the tracking code and web-based services provided by the software [Figures 1 and 2].

Limitations, weaknesses and advantages of hypothyroidism and phenylketonuria screening software

Due to the implementation of this software in Isfahan province and available feedbacks, this section aims to evaluate the advantages, weaknesses and limitations of the screening software. Among the advantages of this software are:

- Reduction of cost of re-sampling by 40%
- Reduction of the necessary human resources by 20 persons per day

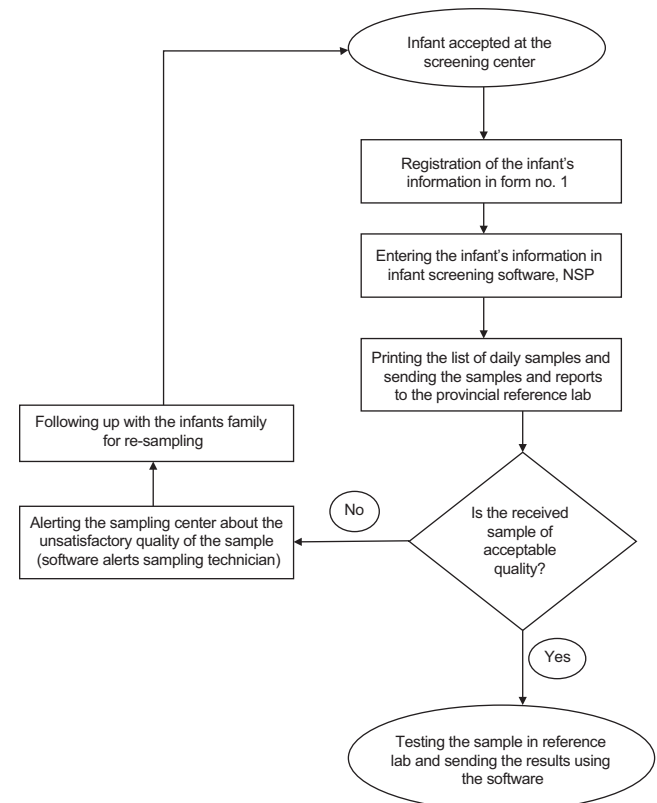


Figure 1: Initial sampling process at the health center

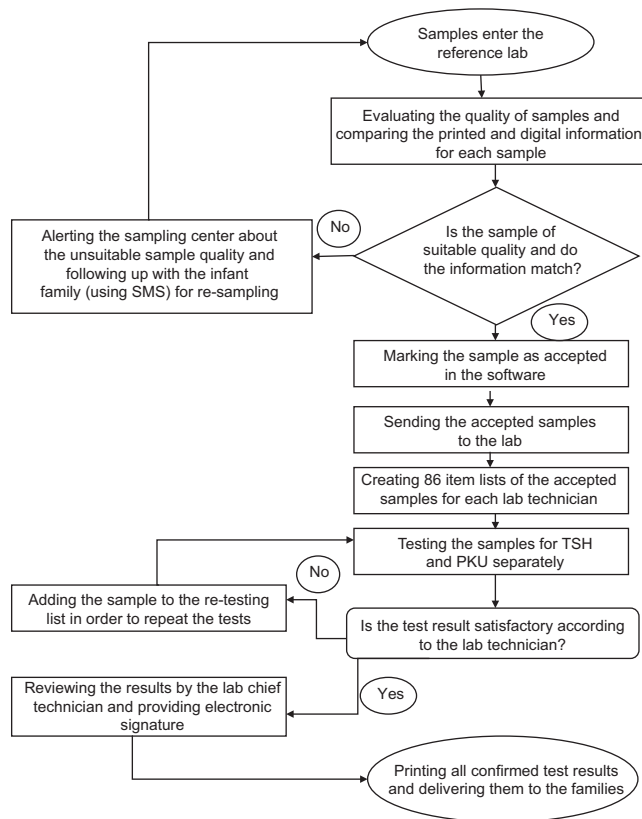


Figure 2: The process of receiving samples, acceptance, Tests carried out on samples And send a response to health centers

- Reduction of costs for phone follow-ups by 20 million Rials per month
- Creation of a comprehensive database containing information about one of the most important health services provided in Isfahan province
- Easy of access and creation of added value by creating monthly, seasonal and annual reports and facilitating long-term planning, reduction of organizational costs, reduction of error, etc.
- The possibility of delivering the written or electronic test results to the patients and with the electronic signature of chief technician of provincial reference lab
- Improving the supervision on the delay between sampling, delivery of samples and testing, which directly effects the results
- Reduction of the time necessary for registration of test results and reduction of necessary human resources
- Elimination of reporting by telephone leading to a reduction of cost and necessary human resources
- Elimination of delays between certain processes such as registration of information and receiving of information from the lab and testing and delivering the results to the sampling center
- Improving the quality and precision of the services provided.

Furthermore, given the fact that the main goal of this screening program is testing all born infants in Isfahan province (100% coverage), if this software was able to

communicate with databases of hospitals or census office and gain access to the number of born infants, it would have been possible to follow-up on infants that are not brought to the testing centers thus decreasing the number of infants that do not undergo the screening. This would lead to (close to) 100% coverage of the screening program.

CONCLUSION

Congenital hypothyroidism or CH is among the most common causes of preventable mental retardation worldwide and is treatable given early diagnosis and treatment.^[12] PKU is another rare congenital metabolic disorder caused by lack of phenylalanine hydroxylase enzyme or its cofactor tetrahydrobiopterin, which results in accumulation of phenylalanine in bodily and neurological fluids. Given the high prevalence of these to disorders among Iranian infants, early diagnosis and treatment of these disorders can greatly reduce the adverse effects on the infants. These adverse effects also create a large financial liability due to the high cost of treatment and care for those suffering from the effects of these disorders, making the early diagnosis and treatment of these disorders a way to save valuable resources.^[13]

Therefore, due to the importance of hypothyroidism and PKU screening program, the computer software for infant screening program was designed and implemented. After the implementation of this software in Isfahan province, there have been improvements in quality and accuracy of the services, reduction of costs, the creation of added value, and creation of a comprehensive database. This software also helps reduce repeated and redundant procedures and necessary human resources, provide the necessary information and statistics for long-term planning and carry out the screening program with minimal amount of error and in the least possible amount of time. Finally given the proven value of this software in the screening process for Isfahan province, it is suggested that the use of this software be implemented nationwide in order to reduce the adverse effects of these disorders.

Suggestions

Finally given the advantages caused by implementation of this software in Isfahan province, it is suggested for this software to be implemented nationwide in order to reduce the adverse effects of these two disorders and improve the precision and quality of the infant screening program in Iran.

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Conflicts of interest

There are no conflicts of interest.

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