IN THE NAME OF GOD
Endocrine & Metabolic Diseases Programs

National Programme for Diabetes Control and Prevention

National Newborn Screening Program for Congenital Hypothyroidism

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Endocrine & Metabolic Disease Office
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Introduction

The rise in diabetics in developing countries (170% increase) is significantly greater than in developed countries (42% increase). Considering numerous, long-term and serious complications of the disease such as ophthalmic, renal, vascular and nervous disorders, which lead to blindness, severe renal failure, amputation and CVA or MI, it can be presumed that several problems and restrictions will be encountered by the expanding population and the individuals at risk, if appropriate and prompt action for prevention, control and treatment of the disease is not taken. The devastative complications of diabetes such as retinopathy, nephropathy and cardiovascular disease are imposing a huge burden on national healthcare services. It is estimated that Diabetes mellitus accounts for between 5-10% of nation’s health budget. Besides, the rate of cardiovascular disorders is very high among these patients, so that CAD and CVA are the most common causes of death in diabetics.

Life style changes can slow the development of diabetes in high risk groups.
Investing in prevention, particularly early detection, in order to avoid the onset of diabetes complications, can significantly reduce the cost of diabetes.

The main goal of implementation of the National program for Diabetes Control and Prevention is to prevent and control of diabetes and its complications.
We believe that this challenge is based on giving educations to healthcare providers, patients, their families and finally the whole community, and also on screening of high risk population for developing diabetes type 2.
National Programme for Diabetes Control and Prevention

**General Strategies**

1. Setting minimum standard of healthcare for control and management of diabetes and required facilities
2. Aid in providing minimum healthcare standard
3. Supporting research on diabetes
4. Aid in expansion of reference laboratories in order to control the quality of diabetes-related tests
5. Aid in providing drugs, equipments and materials required to control diabetes
6. Draw the attention of authorities for financial support
7. Aid in providing insurance for diabetics
8. Aid in providing laboratory equipments with higher standards for health care centers

**The General Objective**

Prevention and control of diabetes and its complications.

**Specific Objectives**

1) Primary prevention
   - Reduction of the incidence and the prevalence of diabetes type 2
   - Reduction of the incidence and the prevalence of risk factors for diabetes type 2 (Obesity-physical inactivity-inappropriate nutrition habits)
**Strategy**

- Modification and correction of the style of individuals at risk and of the whole community, control and reduction of risk factors.
- Identification of individuals with risk factors for diabetes according to guidelines.
- Follow up and management of high risk individuals according to guidelines.
- Raising awareness and understanding of diabetes predisposing factors, their disadvantages and method of prevention and authorities and healthcare providers.
- Raising awareness of the disease, its complications and its natural course in susceptible individuals, community high risk individuals and healthcare providers.

2) **Secondary prevention**

- Prevention, reduction and delay in the incidence of long and short-term complication of diabetes; i.e modification and interruption in the natural course of the disease.

**Strategy**

- Early diagnosis of the disease by screening the individuals at risk and pregnant women, and identification of patients with diabetes type 2 according to guidelines
- Prompt and appropriate management of identified patients in order to control and prevent the disease according to guidelines
• Raising awareness and understanding of the disease and its complications, the method of prevention and control of its complications.
• Diabetes management in populations of diabetics, their families, community and healthcare providers.
• Raising awareness and understanding of other cardiovascular risk factors (e.g., smoking, hypertension, hyperlipidemia, physical inactivity, and obesity) by diabetics, their families, and healthcare providers.

3) Tertiary Prevention

• Reduction of the incidence and delay in appearance of disability and death caused by complications.
• Increasing life expectancy.

**Strategy**

• Screening individuals with diabetes type 2 for the purpose of making early and in time diagnosis of ophthalmic, renal, neurologic, and cardiovascular complications according to guidelines.

**The Final Outcome**

1. Diminished economic costs due to diabetes and its complications
2. Reduced rate of disabilities caused by diabetes and its complications
3. Reduced mortality rate caused by diabetes and its complications
4. Increased life expectancy for diabetics
Treatment goals approved by the National Scientific Committee of diabetes.

The treatment goal is to achieve the conditions stated at this table:

<table>
<thead>
<tr>
<th></th>
<th>Optimal</th>
<th>Satisfactory</th>
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<tbody>
<tr>
<td>FBS (mg/dl)</td>
<td>70-120</td>
<td>&lt; 140</td>
</tr>
<tr>
<td>2-hr postprandial BS (mg/dl)</td>
<td>90-140</td>
<td>&lt;180</td>
</tr>
<tr>
<td>Cholesterol (mg/dl)</td>
<td>&lt;200</td>
<td>&lt;200</td>
</tr>
<tr>
<td>Triglyceride (mg/dl)</td>
<td>&lt;150</td>
<td>&lt;200</td>
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<tr>
<td>HDL* (mg/dl)</td>
<td>&gt;40 in males &lt;50 in females</td>
<td></td>
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<tr>
<td>LDL** (mg/dl)</td>
<td>&lt;100</td>
<td>&lt;130</td>
</tr>
<tr>
<td>Blood pressure (mm hg)</td>
<td>&lt;130/85</td>
<td>&lt;140/90</td>
</tr>
<tr>
<td>FBS in pregnant women (mg/dl)</td>
<td>60-90</td>
<td>&lt;100</td>
</tr>
<tr>
<td>Hb A1C(%)</td>
<td>&lt;7%</td>
<td>&lt;7.5%</td>
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<tr>
<td>BMI</td>
<td>20-25</td>
<td>25-27</td>
</tr>
</tbody>
</table>

Treatment goal of GDM

FBS Optimum: 60-90 One or two hours postprandial BS < 120(mg/dl)

Normal values after ingestion of 100g glucose

(according to Carpenter criteria)

Fasting Plasma glucose → < 95 mg/dl  
BS one hour after OGTT → < 180 mg/dl  
BS two hours after OGTT → < 155 mg/dl  
BS three hours after OGTT → < 140 mg/dl

If two samples of the above are equal or greater, glucose tolerance test is impaired, and the case is diagnosed as GDM. If only one of the four samples shows abnormality, after one month at 32-36 weeks of gestation, a 3-hour-OGTT, using 100g glucose should be performed again. Otherwise she is considered as normal. Pregnant women with GDM should receive intensified attention.
Organization and Executive Process for Diabetes Prevention and Control at Medical University
Four levels of diabetes care

<table>
<thead>
<tr>
<th>4th level Diabetes centre</th>
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<tbody>
<tr>
<td>Internist (endocrinologist), educational nurse, nutritionist, consultant physicians</td>
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<table>
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<tr>
<th>3rd level Diabetes unit</th>
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<td>Internist (endocrinologist), educational nurse, nutritionist, consultant physicians</td>
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<table>
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<tr>
<th>2nd level Diabetes team</th>
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<tr>
<td>General physicians</td>
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<tr>
<th>1st level</th>
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<tr>
<td>Behvarez, karden (with volunteer aid)</td>
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<tr>
<td>- Education of:</td>
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<tr>
<td>- the public</td>
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<tr>
<td>- high risk individuals</td>
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<td>- patients</td>
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<tr>
<td>- Follow-up of:</td>
</tr>
<tr>
<td>- high risk individuals</td>
</tr>
<tr>
<td>- patients</td>
</tr>
<tr>
<td>- Data collecting and reporting</td>
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</tbody>
</table>

| - Screening those at high risk |
| - Early diagnosis of diabetes |
| - Control and treatment |
| - Referral to the next level |
| - Patient screening |
| - Complications |
| - Quality control |
| - Feedback |
| - Education (public, patients) |
| - Data collection and reporting |

<table>
<thead>
<tr>
<th>Health houses and posts</th>
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<tr>
<td>Health centres (rural and urban)</td>
</tr>
<tr>
<td>District hospital</td>
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<tr>
<td>University (provincial hospital)</td>
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Figure 1: Levels of diabetes care provided by the health care system of the Islamic Republic of Iran
1- **Introduction:** Diabetes Mellitus (DM) is a major burden for the health care system and its prevalence is increasing worldwide. DM and its complications consume an enormous part of the health budget in each country. Changes in life and environment are one of the most important causes of increasing in the prevalence of the Metabolic Syndrome. The Metabolic Syndrome consist a cluster of the most important risk factors for cardiovascular diseases (obesity, diabetes, GDM, hypertension, dyslipidemia, etc) and it is the main health problem in the recent century.

2- **Current Situation:** Based on previous researches on Diabetes mellitus in Iran, the Ministry of Health and Medical Education decided to design and practice The National Plan for the Prevention and Control of Type 2 Diabetes Mellitus in Iran. The Advisory Committee was established and the members were selected in 1996. The practical guidelines were designed and the educational materials were edited in order of 7 books. The Educational workshops and seminars were held regarding diabetes mellitus by end of 1997. Then, the program was piloted in 17 universities. National program was evaluated and revised in 2002. Finally, the National Program for Control and Prevention of Type 2 Diabetes Mellitus was implemented and integrated in the Primary Health Care Network in 2004, in whole country. Screening for DM is performing in rural areas actively and in the urban areas passively.

3- **Program Definition:** This report describes results of the DM screening campaign in rural areas of Iran. “WHO” criteria were used for diagnosis of pre-diabetics and diabetics. Gestational Diabetes
Mellitus (GDM) was diagnosed by using the Glucose Challenge Test (GCT) with cut-off point of 140 mg/dl following a standard OGTT (with 100gr Glucose) for confirmation of GDM in suspected cases.

Outcomes & Results:

Educational and practical materials were edited into 7 books for different levels of personnel and distributed among them.

Data from the pilot study of the national program showed the prevalence of type 2 DM in urban areas is equal to 5% and in rural areas is 2.21%. Data from implementing phase of the national program in the country revealed that the DM scenario in Iran is the same with other parts of the world and DM is increasing rapidly.

THE FIRST SCREENING 2004-2005 results

The rural population was approximately 16700000 and the target
population was about 6,000,000 whose were over 30 years of old. 5,882,756 individuals were evaluated for several risk factors.

**SCREENED PEOPLE IN RURAL PARTS OF IRAN 2004-2008**

Participants (~35%) had at least one risk factor for DM and underwent fasting blood glucose test. 51000 were in the pre-diabetic state. Totally, 193000 diabetic patients were founded which 62000 were newly diagnosed. Diabetes
prevalence was 3.30% in rural areas of Iran which is increasing dramatically compared with previous study (3.30% vs 2.21)

**PREDIABETIC PATIENTS 2004-2008**

**ALL DIABETICS 2004-2008**
The Second Screening 2008-2009

Less than 6,000,000 individuals (5950000) were evaluated for several risk factors during the second screening of rural areas in 2008-2009.

2212000 participants (~37%) had at least one risk factor for DM and underwent fasting blood glucose test.

Totally, 237000 diabetic patients were founded which ¼(one-fourth) were newly diagnosed. Diabetes prevalence was 4% during second screening in rural areas of Iran which is increasing dramatically compared with previous studies (4% vs 3.30 and 2.21%). Meanwhile, the prevalence of hypertension in the population during screening in 1387 was equivalent to 6.4%.
Diabetes Program in Cities With More Than 1 Million Population

The second phase of “The National Program for the Prevention and Control of Type 2 Diabetes Mellitus” was implemented in Tehran (capital) and five cities with more than one million person population since April 2010. Target population was 9.2 from all 22 million persons who live in these cities (Tehran-Karaj-Tabriz-Esfahan-Shiraz-Mashhad). Base on the previous researches, Diabetes prevalence in these cities are more than 10% among >30 year old people (approximately one million patients). The first report of phase 2 will be published by April 2012.

The diabetes epidemic has been recognized as the largest and fastest growing in the world right now.
National Newborn Screening Program for Congenital Hypothyroidism in I.R.Iran

Introduction:

The newborn screening (NBS) program, as a preventive medical act, has been implemental for early identification of affected newborns with serious medical disorders. It is a timely intervention causes significant reduction in related disabilities. NBS emerged in the 1960s in the USA and now, an accepted part of routine Neonatal Health Care in all developed and many of developing countries. The policy of NBS and its recommendations varying from country to country and region to region, depending on local economic, political, health priorities, and public health organization. The goal of newborn screening for metabolic and inherited disorders is to identify newborns at risk for certain metabolic, endocrine, hematologic and other conditions that would otherwise be undetected until damage has occurred, and for which intervention and/or treatment can improve the outcome for the newborn.

NSB has been designed based on the primary health care (PHC) network in Iran. PHC is the product of over 3 decades of dedicated efforts, deliberations, innovations and planning. It provides a nationwide primary health care services in the most locally appropriate, well designed and sustainable manner. The NBS program was designed in 2003 and it was piloted in 2004 in 3 provinces and then was reviewed in early 2005, and finally, it was implemented in the Health System in Oct 2005 with testing for
primary congenital hypothyroidism (CH). Saudis showed the cost effective of this programs within the health care system. It has been designed in a few phases in Iran and in each phase, one disease will be added to the NBS panel. CH was chosen to be screened in the first phase, and phenylketonuria (PKU), glucose 6 phosphate deficiency (G6PD), galactosemia, and congenital adrenal hyperplasia (CAH) will be added in further phases. The NBS comprises the sum of the activities (Education, Screening Test, Recall and Confirmation, Diagnosis, Management, Evaluation and Quality Assurance) necessary to ensure that coverage of screening is acceptable, treatment is initiated as soon as possible, and follow-up is adequate and continues to insure a happy and healthy life for each child in the country. The screening laboratories are established in each province and be evaluated regularly by the National Health Laboratory (NHL).

Most neonates born with CH have normal appearance and no detectable physical signs. Hypothyroidism in the newborn period is almost always overlooked and delayed diagnosis leads to the most severe outcome of CH, mental retardation, emphasizing the importance of neonatal screening. It is one of the most common preventable causes of mental retardation. Previous studies in Iran showed that the prevalence of CH is very high in country (4,5,6). The incidence rate of CH had been estimated 1 in 1000 live birth, previously. But it has been revealed that the incidence is at least 2 times more and exact incidence will be known after 3 years of initiating the NBS program. 1.1 – 1.2 million births occurred in Iran per year. The cost / benefit ratio of screening for CH is 1 to 15 dollars in the country.
Methods:

Several effective strategies were employed to achieve the aims of the program. The most important strategies are as follows: public awareness, education and training, early recall with a low positive and no negative rates, early and proper treatment, sustain good metabolic control, program expansion, and applied research. The NBS program was introduced by Ministry of Health and Medical Education for Congenital Hypothyroidism in 2005. All 45 Universities of Medical Sciences have the main responsibility of performing the NBS program in their region. At least each of 30 provinces of the country has one university and some of those have more than two. All 45 medical universities in Iran are involved in this great public health action. I.R.Iran Post Company and Behzisti Organization are the NBS program sponsors. In addition, International Atomic Energy Agency (IAEA) and Atomic Energy Organization of Iran (AEOI) are collaborating with the NBS program in Iran by RAS/6/043-9005 project. Public awareness particularly in pregnant women is one of the most important strategies in this program. Most of pregnant women receive the pre-natal services and the pre-natal care providers give pregnant women informational material regarding newborn screening and educate them twice during gestational period. Additionally, the NBS program has support of several scientific societies and Media to raise professional and public awareness. Parent education is an important part of the program. Education materials for public, parents, health providers, health workers, laboratory technicians, and physicians have produced under supervision of the advisory committee. More than 900
seminars and workshops were held to educate health professionals and more than 7000 physicians, more than 15000 health worker and laboratory technicians and 25000 health workers were educated. More than 6000 centers established for blood sampling from heel of neonates on filter paper. 45 endocrinologist, neonatologist, and pediatrics are practicing as “Focal Points” in this program for scientific supervision and other 300 pediatrics work as consultants in district. In addition, several general practitioners who work at rural areas are also involved in the follow-up of diagnosed CH patients. The NBS laboratories are established in each province and their staffs have been educated and evaluated regularly by the National Health Laboratory (NHL).

**Screening test**

Capillary heel prick is used as sit of sample collection at age of 3-5 days of life on a Guthrie card (filter paper-S&S 903). The samples are sent to the NBS laboratory in the each province by express post. It is highly desirable the blood be collected when the neonate is between 3 to 5 days of age. But there will be situations in which this is virtually impossible. In instances such as critically ill or premature neonates may rescreen within 14 days after births. Thyroid stimulating hormone (TSH) is measured as the screening test. TSH is assayed by ELISA method.
Primary Follow up (Recall and Confirmation)

Inconclusive or positive screen results reported by phone or fax from laboratory to follow-up staff and the health care provider at the specimen taking centers, immediately. Then, the Health care provider contacts baby’s parents and informs them for performing the confirmation tests and the Confirmation Laboratory’s address are submitted to them. Local GPs evaluate the suspicious cases and request the confirmatory tests on serum. The confirmatory laboratories are supervised closely by the Laboratory Affairs Office located at the local university.

Diagnosis: Diagnosis carried out depending on the screen result and on the newborn condition and confirmatory testing. As soon as a diagnosis of hypothyroidism is confirmed, Levothyroxine replacement is initiated based on the NBS guideline.

Limitations of Screening The American Academy of Pediatricians states that: “screening does not equate with diagnosis. Some infants with disorders included in the newborn screening may be missed, even when properly screening performed. It may be due to individual or biological variations. Other infants with CH may be missed due to administrative or laboratory error. Although the pediatrician cannot be held responsible for these problems, he or she must recognize that any child with a negative newborn screening test may still be affected by the disorders. The pediatrician should trust his or her clinical judgment, even in the face of a normal newborn screening report, and should carry out appropriate diagnostic testing if indicated by clinical signs and symptoms”.

Management

Once diagnosis was made the treatment will be started. Parents are received face to face education and written educational materials. In addition, the management team provides appropriate services and regular visits based on the program guidelines.

Evaluation and Quality Assurance: Program evaluation is based on data collection and analysis, long term tracking and outcome evaluation, Cost Benefit Analysis, etc. The quality assurance of the laboratory testing of the NBS program had been established. It is used to refine and enhance all components within the system and containing General NBS System, pre-analytical, analytical, and post-analytical considerations.

Documentation/Data

There are three information forms which are completed during the screening program to gather the data on the NBS program. A computerized database has been developed for the program and it is currently being implemented, but it needs to be carefully reviewed to ensure that it meets all relative record keeping requirements. At present, data is sent to the manager’s office at CDC by CDs from each province every 3 months. But we are planning to develop an online platform for this purpose.

The NBS program Indicators

There are several performance indicators for the NBS program as follow: the NBS program coverage, timely sample collection, timely
TSH measurement at the Screening Laboratory, timely treatment initiation, measures of long-term outcome, and costs associated with treatment. Some of these can be evaluated each season or year and others after 3 years of initiation of treatment. Statistical analysis was done using SPSS Version 11.5 (SPSS Inc, 1989-2002) for windows.

**Results**

Results present data from Oct 2005 till late jun 2011. Totally, 5715914 neonates have been screened (49% females and 51% males). Totally 13696 patients diagnosed and treatment has been initiated in about 99.9% of them. There are a few millions of refugees from Afghanistan and Iraq who live in Iran. To find out the real number of birth, a combination of number birth certification and data from vaccination for tuberculosis (BCG) were used and the greater number of each was used as the real number of birth in each provinces. There is coverage of 94% of the newborns in the country. The recall rate is 3.2% and the parent’s response rate is excellent (99.9%)

**Discussion**

Based on finding of the national NBS program performance in Iran, the coverage and its progression are great. All performance indicators are at acceptable level regarding the age of the program. More than 13000 babies diagnosed with CH and replacement therapy with Levothyroxine has been initiated and follow up is conduction based on the national guideline. These patients are a group of both “permanent” and “transient” forms of CH. Although
transient hypothyroidism may occur frequently all CH patients should be treated for the first 3 years of life, taking into account the risks of mental retardation. Are-evaluation after 3 years is needed in such patients. The rate of CH in Iranian newborns has been high and it has been reported, previously. Several risk factors have been reported for developing CH in neonates including environmental and genetic factors. In other word, environmental, familial marriage, maternal, neonatal, and technical factors may involve in developing CH (both transient and permanent forms). A few studies are performing regarding the high rate of CH and to access the risk factors for developing CH in Iranian newborns, currently. In addition, a genetic study is designing regarding this issue, now.

CH is more prevalent in girls than boys similar to other reports. The CH prevalence is different in countries, and it related to iodine deficiency more than ethical differences. Iodine deficiency is the most important cause of CH worldwide. Iodine is essential for thyroid hormone synthesis and is very important environmental factor in developing CH. It also is necessary for central nervous system especially during the first 3 years of life and iodine deficiency may causes disorders from transient CH to mental retardation. Thyroid gland in neonate is more sensitive to iodine deficiency than their mothers. It is may due to less iodine storage in fetus and neonates and it causes TSH elevation. On the other hand, pregnant women have more sensitivity to iodine sensitivity than non-pregnant. Furthermore, there are several studies which suggest that the NBS program for CH (by using TSH as the screening test) may be used as a suitable indicator foe monitoring and evaluation of the Iodine fortification of foods. According to WHO criteria, TSH level >5 mU/L
resulted from NBS program is more than 3% in iodine deficient regions. Iodine and thyroid function disorders play an important role in thyroid function of newborn. Iodine excess can be another cause of TSH elevation in newborn. It is helpful if the containing antiseptics, particularly iodine tincture, be withdrawn from all obstetrics clinics. Cesarean is another risk factor for developing CH in newborns and in Iran the rate of cesarean is high. Multi-factorial factors are involved in developing CH in newborn. Further investigations are needed to reveal this issue in Iran.

**Conclusion**

The NBS program is one of the most successful actions regarding the Child Health in Iran. Its infrastructure is used as a platform for performing other program for neonates. It will follow the NBS Action Plan and will add other prevalent metabolic diseases on the panel in future. The expansion of the NBS program across the country presents both an opportunity and an obligation for newborn screening professionals, advocates and policymakers to strengthen those components of the newborn screening system needed to support children and families of children who are diagnosed with metabolic diseases. Ministry of health and CDC have provided valuable leadership and all Iranian medical universities have done a great job in conducting the program nationally. These efforts must continue and multiply with a significant commitment of new resources.