

ARTICLE ORIGINAL/ORIGINAL ARTICLE
**COST-BENEFIT ANALYSIS OF G6PD SCREENING
IN LEBANESE NEWBORN MALES**

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Khneisser I, Adib SM, Loiselet J, Megarbane A. Cost-benefit analysis of G6PD screening in Lebanese newborn males. *J Med Liban* 2007 ; 55 (3) : 129-132.

ABSTRACT • INTRODUCTION : G6PD deficiency is one of the most prevalent genetic diseases in Lebanon (1% in Lebanese males). Easy and effective screening methods exist to detect this deficiency early in newborns.

OBJECTIVE : To assess the cost-effectiveness of G6PD deficiency screening in the routine work-up of every male newborn in Lebanon.

METHODS : Of 299 babies with G6PD deficiency detected between 1999 and 2004, 139 (46.5%) were located, contacted, and surveyed for their experience of acute anemia crises.

RESULTS : A previous community survey had indicated a 77.8% risk for an acute anemia crisis necessitating hospitalization in unscreened patients, most often associated with consuming fava beans raw or in combination products. In contrast, only 5 (3.8%) of the 139 screened G6PD-deficient babies had ever developed a severe acute anemia crisis. The risk for hospitalization following a crisis had thus been reduced by 95% among patients screened for G6PD deficiency, compared to those unscreened. The estimated mean cost of each hospitalization, which lasts on average 7 days, is 1450 USD. The cost of screening is about 3 USD. The analysis indicates that, given the current prevalence of the deficiency and the reduction in hospitalization rates associated with knowing one's status, the cost of systematic screening is about 2.58 times lower than that of anemia-related hospitalizations in an unscreened population.

CONCLUSION : The efficiency of routinely testing evidenced here supports changes in screening policies for boys.

INTRODUCTION

A seminal screening technique for G6PD (Glucose-6-Phosphate Dehydrogenase) deficiency was first proposed and standardized by Beutler in 1979 [1]. Several improved modifications, like the Solem modification (1985) for example, have since become available on the

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RÉSUMÉ • INTRODUCTION : Le déficit en G6PD est une des maladies génétiques les plus fréquentes au Liban (1% des garçons). Il existe des méthodes simples et efficaces qui en permettent un dépistage précoce chez les nouveau-nés.

OBJECTIF : Analyse « coût-bénéfice » du dépistage néonatal du déficit en G6PD chez les garçons au Liban.

MÉTHODES : Des 299 bébés dépistés déficitaires en G6PD entre 1999 et 2004, 139 (46,5%) ont été localisés, contactés et enquêtés sur leur expérience de crises d'anémie hémolytique sévère.

RÉSULTATS : Une étude antérieure avait révélé un risque de 77,8% de survenue d'anémie hémolytique sévère nécessitant une hospitalisation chez les sujets non dépistés. Ces crises sont souvent associées à la consommation de fèves fraîches et leurs dérivés. Seulement 5 (3,8%) des 139 bébés dépistés déficitaires ont jusqu'à présent développé une crise hémolytique sévère. Le risque d'hospitalisation suite à une crise a donc été réduit de 95% parmi les patients dépistés en comparaison avec ceux non dépistés. Le coût moyen de l'hospitalisation, avec une durée moyenne de 7 jours, est estimé à 1450 US\$, celui du dépistage est de 3 US\$. L'analyse prouve, en tenant compte de la prévalence du problème et de la réduction des taux d'hospitalisation occasionnée par la connaissance du statut de porteur, que le coût d'un dépistage systématique est 2,58 fois moins important que le coût des hospitalisations qui surviendraient dans une population vierge de tout dépistage.

CONCLUSION : L'efficacité du dépistage systématique est évidente et plaide pour l'adoption d'une politique de dépistage chez les garçons.

market [2], and are currently widely used in many screening programs worldwide [3-8]. In Lebanon, a Center for newborn screening of CH, PKU, and G6PD was launched ten years ago. Actually, it covers 20% of the total newborns in Lebanon. Between 1996 and 2004, a cumulative G6PD deficiency incidence of 0.5% was found among about 95,000 babies screened [4] using a

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modified G6PD analysis method [1-2] approved by an External Quality Assurance Program [3]. This incidence was significantly higher among males (1%) versus females (0.04%) [4]. In addition to its elevated frequency, G6PD deficiency in Lebanon is also characterized by its relative severity [9-11]. Early acute anemic crises have historically been triggered in patients unaware of their genetic conditions by the consumption of raw green fava beans ("favism"), a practice common among Lebanese [4, 12-14]. If a screened baby is diagnosed with G6PD deficiency on a recall sample (PPV > 95%), parents are notified by the pediatrician and receive a list of drugs and food items to be avoided to prevent acute anemic crises. Without screening, no such preventive education is possible.

The relatively higher incidence of G6PD deficiency, the frequency in the community of a risk factor leading to associated anemia crises, and their relatively severe clinical presentations suggest that G6PD screening should become a mandated routine test for newborns. This study aims at reinforcing this suggestion by providing a cost-benefit analysis, which may add an argument towards the policy change we advocate. The analysis included only males in view of the major predominance of the disorder in that sex.

METHODS

Sources of data

This cost-effectiveness analysis used several sources of data :

1. A description of previously undetected G6PD-deficient cases in a random survey of the general population [4].
2. An interview with families of babies screened at the Center between 1999 and 2004 (see methodology below).

Participants and procedures

In September 2005, records of boys diagnosed as G6PD deficient cases between 1999 and 2004 were retrieved. Families whose accurate phone number was found in the record were contacted. The purpose of the study was explained to an adult responsible member. Although it was clearly stated that the family was free to participate or not, none of those contacted refused to do so.

A history of occurrence of an acute anemic crisis following diagnosis was obtained. For each child who had suffered an acute anemic crisis, age at time of crisis and the triggering factor of that crisis were assessed. The approximate direct cost and duration of hospitalization during those crises were also obtained.

Plan of analysis

The proportion of crises avoided by screening per 100,000 persons was calculated from the proportion of crises reported in unscreened cases minus those reported in the screened ones. Subsequently, the total cost of

those crises avoided was calculated. This total cost was compared to the total cost of detecting G6PD deficiency cases in 100,000 screened babies. A cost-effectiveness index was computed by dividing the benefits measured by costs saved from avoided crises over the cost of screening. The index of an efficient intervention should exceed 1. An index lower than 1 is an indication of an inefficient intervention.

RESULTS

1. G6PD-related anemic crises in unscreened cases

In 2005, a community-based survey of 3000 males 15 years old, had revealed that at least one acute anemia crisis necessitating hospitalization had occurred in 77.8% of 36 previously unscreened G6PD deficient patients. The mean age of the first crisis was 4.2 years (SD = 2.4) [4].

2. G6PD-related anemic crises in screened cases

Over the six-year period of this review, 299 G6PD deficient male babies were detected. We were able to successfully contact families of 139 cases (46.5%). At the time of the review, those 139 deficient boys had a mean of age at 3.7 years (SD = 1.4). There was no age difference between the 139 located cases and the other cases, as retrieved from the records. From those 139 cases only 5 (3.8%) had developed an acute anemia crisis. Thus the reduction of hospitalization risk compared to unscreened boys was 95%. The mean age of those crises was 3.6 years (SD = 1.7).

The mean cost per hospitalization was 1450 USD (SD = 700.2) and the mean duration of stay was 7 days (SD = 4). Four of reported crises were directly related to the ingestion of raw fava beans provided by close family members who were not aware or had forgotten the boy's diagnosis. Another case was due to eating deep-fried "falafel" made from a mixture of fava ("foul") and garbanzo ("hommos") beans.

3. Cost-effectiveness of screening

With screening, an excess of 740 hospitalizations (778 in unscreened boys – 38 in screened boys) will be avoided for every 1000 cases of G6PD deficiency, between the ages of 3 to 4 years. The detection of those 1000 cases would require testing 100,000 babies as the incidence in boys in Lebanon is 1%.

At the rate of 3 USD per screening test, the total cost of screening 100,000 boys and subsequently avoiding 740 hospitalizations is therefore 300,000 USD. Thus it costs the community $300,000/740 = 405.4$ USD to avoid one hospitalization of a G6PD deficient boy. This compares favorably with the mean cost of hospitalization, i.e. 1450 USD.

Consequently the cost-benefit index of screening to avoid hospitalization is :

$$\frac{\text{Savings from hospitalization avoided}}{\text{Total cost of screening}} = \frac{(1450 - 405.4)}{405.4} = 2.58$$

DISCUSSION

The effectiveness of exhaustive neonatal screening for G6PD deficiency in any given community depends on :

1. the prevalence of this genetic defect ;
2. the clinical severity of adverse effects which may result from ignoring the diagnosis ;
3. the overall cost of the screening versus that of remediation of adverse effects.

G6PD deficiency is currently one of the most frequently diagnosed genetic defects in boys in Lebanon [14]. Traditional consumption of fava beans either raw or cooked in "falafel" is prevalent, rendering the occurrence of anemic accidents a present possibility in deficiency cases. Those accidents often lead to hospitalizations, which entail direct and indirect costs. Consequently, screening for G6PD deficiency may have a positive preventive impact on newborns. It has been shown that establishing an early diagnosis reduces the risk for hospitalization [5-7]. In our results, this reduction was found to be of 95% among Lebanese boys. A simple equation clearly indicates that costs of testing are largely offset by costs of hospitalizations avoided among screened boys. The evaluation of the advantage did not even include loss of income, and moral and physical hardships to patients and their families. Thus it appears that global testing for boys in Lebanon is a cost-effective intervention.

The age differential between the screened and unscreened populations is directly related to the history of the introduction of the screening test in Lebanon, which does not extend beyond the past 15 years [1-2]. No screened person in Lebanon could therefore be older than 15 years. Conversely, unscreened persons will become older as time passes and be replaced by increasingly smaller age-cohorts. One can even predict a time when the present analysis would become impossible as unscreened persons become less common. Nevertheless, the age differential of the first G6PD-related anemic attack among boys screened or not did not exist. Most children will suffer this crisis within the first 3-4 years of life. After that "alarm" call, the family becomes acutely aware of the existence of the problem and relapses become extremely rare

The effectiveness of universal testing for baby girls may be more controversial, as the incidence of G6PD deficiency is 25 times lower in girls than in boys. Screening a population with such a low prevalence would decrease the predictive value by increasing the rate of false-positives. Any reduction of overall marginal costs of the test brought about by the increased volume of activities may thus be offset or even overturned. Screening may have to be limited to girls in families with history of G6PD transmission.

Larger utilization of testing facilities can lower the price of a single test in a major way. In Greece, where G6PD routine screening was added to a pre-existing uni-

versal newborn screening program in the late 1980s, the overall price decreased to as low as 0.90 USD [5]. In contrast, our current rate in Lebanon, which is about 3 USD, remains relatively elevated but amenable to major reduction. Thus a global screening of all boys will definitely increase the overall cost-effectiveness of this test.

At this point, and based on this evidence, it is strongly recommended to adopt policies for mandatory screening of all male newborns in Lebanon for G6PD deficiency. This is better accomplished through the adoption of this procedure in the national guidelines for postnatal care, which are currently under review.

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دراسة الجدوى الاقتصادية للكشف المبكر لقصور الانزيم غلوكوز ٦ فسفات منزوع الهيدروجين (G6PD) عند الوليدين الذكور في لبنان

ملخص : مدخل - قصور الانزيم (G6PD) هو مرض وراثي منتشر في لبنان : ١٪ من الذكور توجد طرق بسيطة وفعالة تسمح بالكشف المبكر عند حديثي الولادة.

الهدف - دراسة الجدوى الاقتصادية للكشف المبكر لقصور الانزيم عند الوليدين الذكور اللبنانيين.
الطرق - من بين ٢٩٩ وليدا كشف عندهم قصور الانزيم بين ١٩٩٩ - ٢٠٠٤ (٤٦,٥ ٪) جرى الإتصال بهم بغية التحقيق عن نوبات انحلال الدم الشديد لديهم.

النتائج - دراسة سابقة اظهرت خطرا نسبة ٧٧,٨ ٪ لحدوث انحلال دم شديد الذي يحتاج للإستشفاء للذين لم يكشف عندهم نقص الانزيم، تتزامن غالبا نوبات انحلال الدم مع تناول الفول الاخضر ومشتقاته. فقط ٥ (٣,٨ ٪) من ١٣٩ طفل كشف عندهم سابقا نقص الانزيم تعرضوا لنوبة انحلال دم شديد خطر الاستشفاء التالي للنوبة تناقص ٩٥ ٪ عند من كشف عندهم سابقا نقص الانزيم نسبة لمن لم يكشف عندهم نقص الانزيم. تكاليف الاستشفاء بمعدل ٧ ايام طبابة تقدر بمبلغ ١٤٥٠ دولارا اميركيا بينما التحري عن الانزيم كلفته ٣ دولارات : الدراسة تبين اذا اخذنا بالإعتبار انتشار الحالة وتناقص نسبة النوبات التي تحتاج للإستشفاء بان تكاليف الكشف مسبقا هي ٢,٥٨ مرة اقل من تكاليف الاستشفاء لمن تحدث له نوبة انحلال دم شديد بدون كشف مسبق عن الانزيم.

الخلاصة - ان وضوح اهمية الكشف المنظم تشير الى إعتقاد تغير سياسات الكشف المبكر عن الانزيم عند الاطفال الذكور.