Prevalence of G6PD Deficiency in Iran, a Mata-analysis

Mahmood Moosazadeh[1], Mohammadreza Amiresmaili[2], and Maryam Aliramezany[3*]

[1] Department of Epidemiology, Research Center for Modeling in Health, Institute for Futures Studies in Health, Kerman University of Medical Sciences, Kerman, Iran

[2] Department of Health services management, Research Center for Health Services Management, Institute for Futures Studies in Health, Kerman University of Medical Sciences, Kerman, Iran

[3] Department of Cardiology, Medical Informatics Research Center, Institute for Futures Studies in Health, Kerman University of Medical Sciences, Kerman, Iran

Received: 30 Jan. 2013; Accepted: 21 May 2013

Abstract- Search results show that numerous primary studies have been carried out in different parts of Iran regarding prevalence of G6PD deficiency; if results of these studies are combined, a reliable estimation of prevalence of this factor will be achieved in Iran. Thus, present study, aimed to determine the prevalence of G6PD deficiency by combining findings of qualified primary studies using meta-analysis and taking into account heterogeneity considerations. Searching the relevant keywords in Iranian and International databases, primary studies were selected. After quality appraisal and applying inclusion and exclusion criteria, relevant primary studies were selected. In each study, standard error of prevalence of G6PD was calculated according to binominal distribution formula. Finally, heterogeneity index was determined among studies using Cochran's test. Prevalence of G6PD in Iran was estimated by STATA software ver 11 using fixed or random effect model based on heterogeneity results. 148916 subjects in 36 primary studies which entered this meta-analysis were examined. G6PD deficiency prevalence was 6.7% in Iran (men: 8.8% and women: 2.2%). Also, this deficiency in the present study was four times higher in men than in women. Its prevalence was adjusted in different parts of Iran and it was shown that it was between 0.8 and 15.2 using Bayesian analysis. This meta-analysis showed that Iran is among countries with high frequency of G6PD deficiency and there is a significant difference in prevalence of G6PD in different parts of Iran. According to these results, screening newborn children seems very vital. Carrying out other primary studies regarding prevalence of G6PD seems unnecessary.

Acta Medica Iranica, 2014;52(4):256-264.

Keywords: G6PD; Hemolysis; Meta-analysis; Icteric newborn; Jaundiced; Newborn; Iran

Introduction

G6PD (Glucose-6-phosphate dehydrogenase) is one of the most important body enzymes with different cells like red blood cells have different levels of it. Its deficiency is the most prevalent genetic deficiency, which 400 million people in the world suffer from. It was first diagnosed in 1956, and since then numerous studies have been carried out about its different types by scientists (1-4).

G6PD is the first enzyme of hexose monophosphate pathway whose main role is to protect red blood cells against oxidants and to protect sulfidril groups of proteins through glutathione reduction. G6PD deficiency is an X-linked congenital disorder which has different clinical manifestations including icteric newborn, hemolysis and acute icteric following exposure to chemical substances and pharmaceuticals; anemia and acute icteric following exposure to fava bean (favism); and chronic congenital non-spherocytic hemolytic anomia (1,5-6).

G6PD deficiency varies in terms of diversity and variety. Studies have reported that prevalence of G6PD deficiency in Pakistan, UAE, Saudi Arabia, Kuwait, Bahrain, Oman, Egypt and Iran is 2-8, 11, 2-26, 19, 21, 27, 1 and 11.5% respectively (1,7). According to these studies, Iran is among countries with high frequency of G6PD deficiency and its prevalence is different in different parts of Iran. For example, in a study on 2501 screened infants in Esfahan (center of Iran) and Boushehr (south of Iran), G6PD prevalence was 3.2 (boys: 5.1% and girls: 1%) and 8.4% (boys: 14.7 and girls: 2%) respectively (2-3).

Corresponding Author: M. Aliramezany
Medical Informatics Research Center, Institute for Futures Studies in Health, Kerman University of Medical Sciences, Kerman, Iran
Tel: +98 341 3205157, Fax: +98 341 3205222, E-mail address: maliramezany@yahoo.com

Preliminary electronic search and researchers' experiences revealed that numerous studies have been carried out in different parts of Iran regarding prevalence of G6PD deficiency and different levels of this deficiency have been reported. Unfortunately none of these studies are used by executives because, the results are very heterogeneous and no precise and reliable figure on the prevalence of G6PD deficiency is available. Additionally, researchers do similar studies relying on the same methodology and study design to determine that prevalence again and again which means wasting scarce research resources. Thus, if one can provide an acceptable and convincible estimation based on the results of these studies, the necessity of further studies in this regard may fade out.

One of the most important research methods which help us to provide the best estimation for prevalence of a phenomenon in a society is systematic review and meta-analysis. Although previously meta-analysis was only used for combining clinical trials, it is now common to use it for aggregating results of observational (descriptive-analytical) studies on various phenomena (8), e.g. this method has been used to determine the prevalence of G6PD deficiency elsewhere (9). But in Iran, such a study to combine the results of numerous studies on the prevalence of G6PD deficiency have not been carried out, so we decided to present a reliable estimation of prevalence of G6PD through extracting and collecting all available reports, documents and studies using systematic review methods and combining their results using a meta-analysis taking in to account, heterogeneity considerations; in this case, evidence-based decision-making will be provided for planning and policy making and it would tell us if it is necessary to do further research on prevalence of G6PD deficiency.

Materials and Methods

The present study is a systematic review and meta-analysis to determine prevalence of G6PD deficiency in Iran which was carried out relying on documents review.

Search strategy

To retrieve studies published electronically between 21/03/1997 and 30/11/2012, articles published in foreign and domestic journals, dissertations available from Persian information databases of SID, Irandoc, Iranmedex, Magiran, Medlib, and English databases of Pubmed, Google scholar and WHO Site were searched. For this search, we used Persian and English keywords or a probable combination of important, main and critical words. We searched the keywords of "glucose 6 phosphate dehydrogenase deficiency or G6PD deficiency, Jaundice, Neonatal, Prevalence, epidemiology, Blood transfusions, hemolysis, Iran/Iranian, and their Persian equivalents"; between 15/11/2012 and 29/03/2012. Reference of the published studies was also checked to increase sensitivity and to choose more studies. The search was evaluated randomly by one of the researchers to ensure no study has been excluded. Meanwhile, to access findings of unpublished studies, we corresponded with experts and experienced people in this field; unfortunately, no unpublished study was found.

Study selection

Full text or abstract of all retrieved articles, documents and reports were extracted. After studying titles, repeated items were excluded. It's worth mentioning that to avoid probable data republication bias, findings were cross examined by researchers to recognize and exclude repetitive studies. Then, full texts of articles were carefully studied and the relevant articles were selected.

Quality evaluation

After determining the relevant studies, in terms of title and content, eight item STROBE checklist including questions such as "suitable sample size, statistical population, G6PD measuring method, statistical analysis, geographic area of the study, research objectives, presentation of findings suitably and presentation of results based on objectives" was applied to evaluate quality of documents, with one score for each question. Every article which obtained at least 6 scores could enter meta-analysis. Since we didn't intend to enter the score of "study quality" as an independent variable in meta-regression model, we ignored questions like "carrying out a research by a member of well known university or organization, carrying out a research by an expert or experienced person and publication of the article in a well-known journal with high impact factor, etc."

Extracting data

Data was extracted by researchers in terms of "article title, corresponding author, year of the study, total sample size, sample size disaggregated by gender, place of the study, G6PD prevalence index, prevalence of G6PD in terms of gender, age group, study population, blood sampling method and G6PD level measuring method" and entered in an Excel spreadsheet.

Study inclusion criteria

After the evaluation process and obtaining necessary

score, all Persian and English studies which had determined prevalence of G6PD in Iran were selected.

Study exclusion criteria

Following the preliminary search, some of the irrelevant studies were extracted after studying their titles, some after studying abstracts and some others after studying the full texts. Quality of the remaining articles was evaluated against STROBE checklist and those achieved scores less than six were also excluded.

Analysis

To analyze data, Stata Software was used. Standard error of prevalence of G6PD was calculated in every study according to binomial distribution formula. Finally, Cochran's test was used to determine heterogeneity index among primary studies. Based on heterogeneity results (with Meta command in meta-analysis), fixed and random effect models were used to estimate prevalence of G6PD in Iran in terms of gender (man & woman). To minimize random variation, point estimation of findings of all studies were calculated using adjusted Bayesian analysis. Finally, meta-regression method was used to study the effects of variables which were determined as probable causes of heterogeneity in studies. Point estimation of G6PD deficiency prevalence with Confidence interval of 95% was calculated in forest plots; in this plot, square size showed weight of every study and lines in its both sides showed Confidence interval of 95%.

Results

Using relevant keywords, synonyms and "or "operator, the maximum sensitivity was achieved for selecting articles and documents (1648articles retrieved in the first stage). Using "and operator "and increasing search specificity, 388 relevant articles were selected whose abstracts were examined and 294 articles were selected. Of them, 175 ones were excluded due to database overlap and being repetitive. After reviewing full text of the remaining articles, 82 articles were excluded because they weren't related to objectives of this meta-analysis. Quality of all 37 remaining articles was evaluated using the eight item STROBE checklist; one study was excluded because its quality was low and it couldn't achieve the minimum score; two other studies with repetitive findings were excluded. Moreover, two more relevant articles were found after searching the references of the articles. Usanga study (7) which examined prevalence of G6PD deficiency in 6 Kuwaiti, Egyptian, Iranian, Syrian, Lebanese and Jordanian groups who lived in Kuwait was also excluded because it wasn't qualified (Figure 1).

Since primary studies focused on three groups of "icteric newborns, newborn general screening at the day of birth or 3-7 days after birth and other groups (blood donors, students and participants of pre-marriage blood sampling), description of these primary studies and results of this meta-analysis are presented both totally and in terms of all three groups (Table 1 and 2). Total sample size in primary studies entered this meta-analysis was 148916 subjects (73522 men and 64679 women, gender of others was unknown).

Totally 10465 infants were examined regarding prevalence of G6PD in all 14 studies that focused on icteric children; of them, 3039 infants were boys and 3575 ones were girls and gender of others was unknown. Among studies entered this meta-analysis, prevalence of G6PD in icteric newborns varied from 2.1% in both genders in Koosha's study (Zanjan, 2007, 376 sample size) to 16% in Firooz Raji's study (Tehran, 2001, 1500 sample size); regarding icteric boys, incidence of G6PD varied from 4.4% in Koosha's study (Zanjan, 2007, 159 sample size) to 30.7% in Firooz Raji's study (Tehran, 2001, 650 sample size); concerning girls, it varied from 0.5% in Koosha's study (Zanjan, 2007, 217 sample size) to 4.7% in Firooz Raji's study (Tehran, 2001, 850 sample size). Ratio of boys to girls with G6PD varied from 3% in Ahmadi's study (Mazandaran, 2008, 1018 sample size) to 10% in Haj Ebrahimi's study (Tehran, 2004, 2000 sample size). According to results of this meta-analysis, total prevalence of this factor in icteric infants, boys and girls is 6.9, 10.8 and 2.4% respectively (Table 1 and 2).

9 studies examined G6PD deficiency in 127622 newborns on day of birth or 3-7 days after birth (screening); of them, 64026 infants were boys, 60568 ones were girls and the remaining gender were unknown. prevalence of G6PD in this group varied from 0.8% in Mohammadzade's study (Mashhad, 2009, 2570 samples, samples taken from cord blood) to 8.7% in Zahedpasha's study (Babol, 1999, 2046 sample size, samples taken from cord blood); concerning boys, it varied from 1% in Mohammadzade's study (Mashhad, 2009, 1307 samples, samples taken from cord blood) to 14.7% in Movahed's study (Mazandaran, 1997, 190 samples, samples taken from cord blood); concerning girls, it varied from 0.5% in Mohammadzade's study (Mashhad, 2009, 1263 samples, samples taken from cord blood) to 4.2% in Alidalki's study (Rafsanjan, 2007, 495 samples, heel prick blood sampling). Ratio of boys to girls with G6PD varied from 1.4% in Alidalki's

study (Rafsanjan, 2007, 1018 samples, heel prick blood sampling) to 8% in Khalesi's study (Tehran, 2012, 450 sample sizes, samples taken from cord blood).

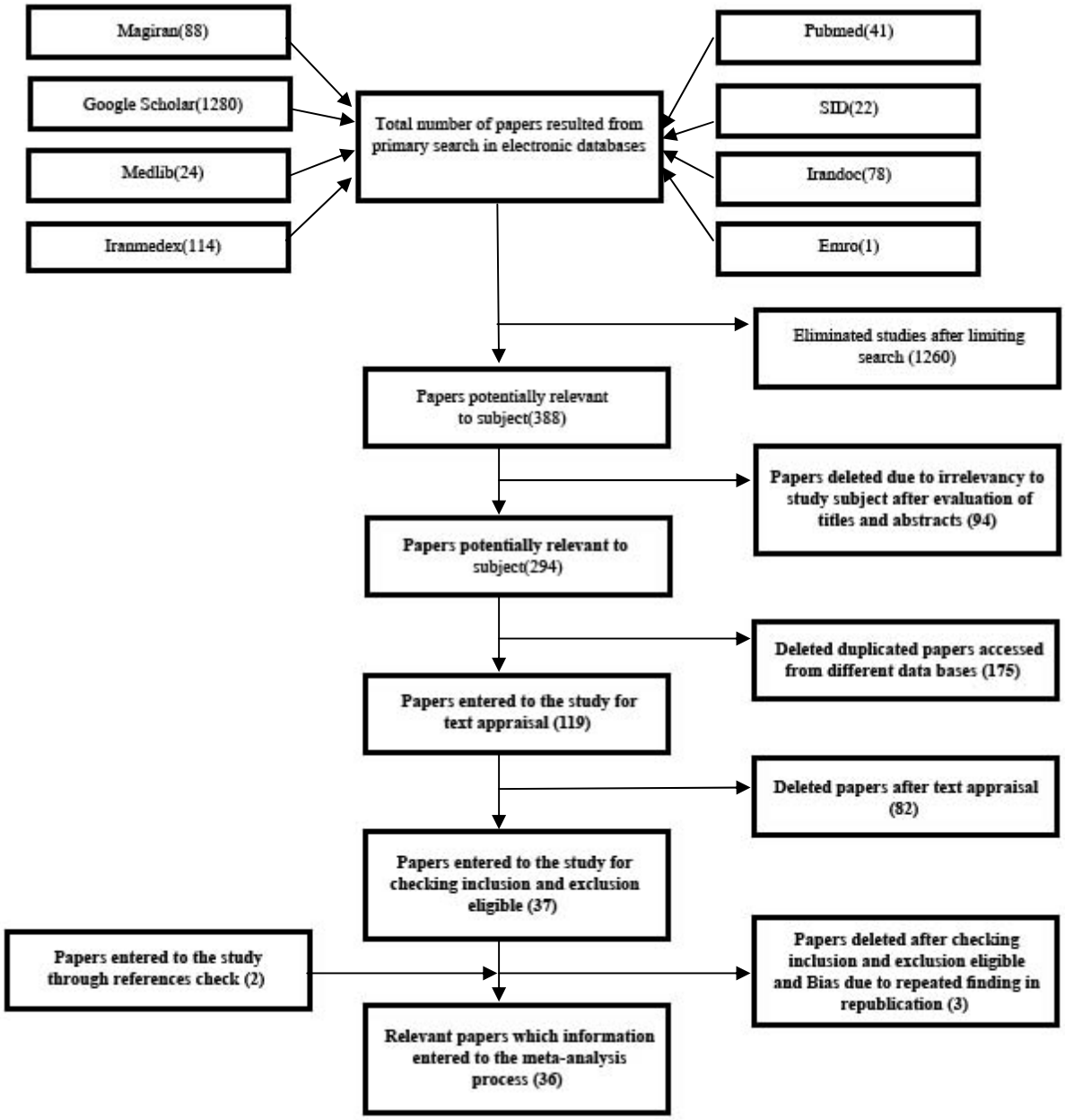

Figure 1. Papers search and review flowchart

According to results of this meta-analysis and based on screening findings, total prevalence of this factor on birthday or 3-7 days after birth in whole and in terms of boys and girls was 4.9, 7.9 and 2.1% respectively. In other groups (blood donors and students, etc.), 10829 subjects were tested (6457 men, 536 women and others were unknown). Prevalence of G6PD in entire study population in this group varied from 5.1% in Mortazavi's study (Sistan Va Balouchestan, 2010, 1805 sample size) to 16.3% in Emam Ghorashi's study (Jahrom, 2010, 706 samples); regarding men, it varied from 2.2% in Mortazavi's study (Zanjan, 2005, 1500 sample sizes) to 15.1% in Karimi's study (Fars, 2010, 79 samples). Only three studies (among non- neonates groups) reported its prevalence separately for women; with its prevalence in studies carried out by Karimi (Fars), Hashemi (Amol) and Mehrabani (Fars) 0, 1.4 and 5.5% respectively. Ratio of boys to girls with G6PD was 1.7 in Mehrabani's study and 7.2 in Hashemi's study. According to results of this meta-analysis, total prevalence of this factor in

other groups in terms of sexes, males and females is estimated at 9.1, 7.2 and 1.5 respectively (Table 1, 2).

Table1. Description of the studies included in the meta-analysis

Population Study	Authors	Year of Publication	Site of Study	Blood Sample	Samplesize (Total)	Sample Size (Male)	Sample Size (Female)	Prevalence (Total)	Prevalence (Males)	Prevalence (Females)	Male/Female Ratio	Score of Quality
Icteric Newborns	Yosofi(9)	2006	Mashhad	VB	505	--	--	6.7	--	--	5.8	6
	Hajiebrahimteheani(10)	2004	Tehran	VB	2000	744	1256	4.4	6.4	1.1	10	7
	Hajiebrahimteheani(11)	2004	Tehran	VB	573	349	224	5.8	8.02	2.2	5.6	6
	Khalili(12)	2003	Rasht	VB	1190	605	585	6.4	9.8	3.1	3.3	7
	Hashemieh(13)	2000	Arak	VB	332	--	--	6.02	--	--	-	6
	Ahmadpoor(14)	2001	Gorgan	VB	326	--	--	5.8	--	--	8.5	6
	Eghbaleyan(15)	2007	Hamadan	VB	272	--	--	4.4	--	--	5	6
	Koosha(3)	2007	Zanjan	VB	376	159	217	2.1	4.4	0.5	7	6
	Nobahar(16)	2003	Semnan	VB	270	177	93	4.4	5.6	2.1	5	6
	Boskabadi(17)	2010	Mashhad	VB	1139	--	--	5.2	--	--	7.4	7
	Ahmadi(18)	2008	Mazandaran	VB	1018	--	--	13.6	--	--	3	6
	Sarreshtehdari(19)	2003	Arak	VB	259	--	--	8.1	--	--	9.5	6
	Firoozrai(20)	2001	Tehran	VB	1500	650	850	16	30.7	4.7	5	7
	Iranpoor(21)	2003	Esfahan	VB	705	355	350	7.5	11.3	3.7	3.1	7
	Zahedpash(22)	1999	Babol	CD	2046	1025	1011	8.7	12.5	4.1	3.1	7
	Movahed(23)	2003	Booshehr	CD	415	190	207	8.4	14.7	1.9	7	6
Newborn	Iranpoor(2)	2008	Esfahan	HPBS	2501	1307	1194	3.2	5.1	1	5.6	7
	Mohammadzadeh(24)	2009	Mashhad	CD	2570	1307	1263	0.8	1	0.5	2.2	7
	Kosaryan(25)	2011	Mazandaran	HPBS	115622	59429	56193	6.1	14.2	3	6.2	7
	Abolghasemi(26)	2003	Tehran	CD	2000	--	--	2.1	--	--	6	7
	Khalesy(27)	2012	Tehran	CD	450	245	205	2	3.3	0.5	8	6
	Mahdavi(28)	1997	Mazandarn	CD	1000	--	--	8.6	--	--	4.7	6
	Alidalaki(29)	2007	Rafsanjan	HPBS	1018	523	495	5	5.7	4.2	1.4	7
	Mortazavi(30)	2005	Zanjan	VB	1500	1500	--	--	2.2	--	--	7
	Hashemi(31)	2002	Amol	VB	732	295	437	5.3	11.2	1.4	7.2	6
	Mirzaei(32)	2000	Yasooj	VB	300	300	--	--	12.7	--	--	6
Others	Mortazavai(33)	2010	Zanjan and Sistan-Balo	VB	1805	--	--	5.1	--	--	--	7
	Rahimi(34)	2008	Kermanshah	VB	1000	1000	--	--	5.3	--	--	7
	Mehrabani(35)	2009	Fars province	VB	152	79	73	7.2	8.9	5.5	1.7	6
	Karimi(36)	2010	Fars province	VB	79	53	26	10.1	15.1	0	--	6
	Nakhaei(37)	2009	Zahedan	VB	1340	1340	--	--	5.9	--	--	7
	Nakhaei(38)	2012	Zahedan	VB	1440	1440	--	--	7	--	--	7
	Nabavizadeh(39)	2007	Yasooj	VB	261	--	--	14.2	--	--	--	6
	Amoozegar(40)	2005	shiraz	VB	450	450	--		6	--	--	6
	KazemiNezhad(41)	2009	Ahvaz	VB	1064	--	--	7.5	--	--	--	7
	Emamghorashi(42)	2010	Jahrom	VB	706	--	--	16.3	--	--	--	6

VB: Venous Blood, CD: Cord Blood, HPBS: Heel Prick Blood Sampling

Table2. Result of meta-analysis the primary study based on Population study and total, Male, Female

population study	Combined of result	Total	Male	Female
Icteric Newborns	**Prevalence of combined**	6.9 (4.9-8.8)	10.8 (5.3-16.3)	2.4 (1.2-3.6)
	Heterogeneity(Q)	210.7	166.3	35.5
	***P*-value**	0.0001	0.0001	0.0001
Newborn	**Prevalence of combined**	4.9 (2.8-6.9)	7.9 (1.9-14.1)	2.1 (0.9-3.3)
	Heterogeneity(Q)	991.6	1990	201
	***P*-value**	0.0001	0.0001	0.0001
Others	**Prevalence of combined**	9.1 (6.2-12.02)	7.2 (5.1-9.4)	1.5 (0.4-2.6)
	Heterogeneity(Q)	74.2	96.5	2.4
	***P*-value**	0.0001	0.0001	0.3
Total	**Prevalence of combined**	6.7 (5.5-7.8)	8.8 (5.8-11.8)	2.2 (1.4-2.99)
	Heterogeneity	1307.6	2765	261
	***P*-value**	0.0001	0.0001	0.0001

Moreover, according to the present meta-analysis, total prevalence of G6PD, prevalence in males and in females was 6.7, 8.8 and 2.2% respectively (Table 2). To study the effects of variables suspicious to heterogeneity, variables including "study place, study population and blood sampling method for measuring G6PD level" were reviewed using single-and multi-variable analysis in meta-regression model; of them, only study place was considered main source of heterogeneity (*P*-value=0.03) (Table 3).

Meanwhile, G6PD level was measured in all primary studies using FST (Florescent Spot Test) method. To review its deficiency, blood sampling method was also described in table 1.

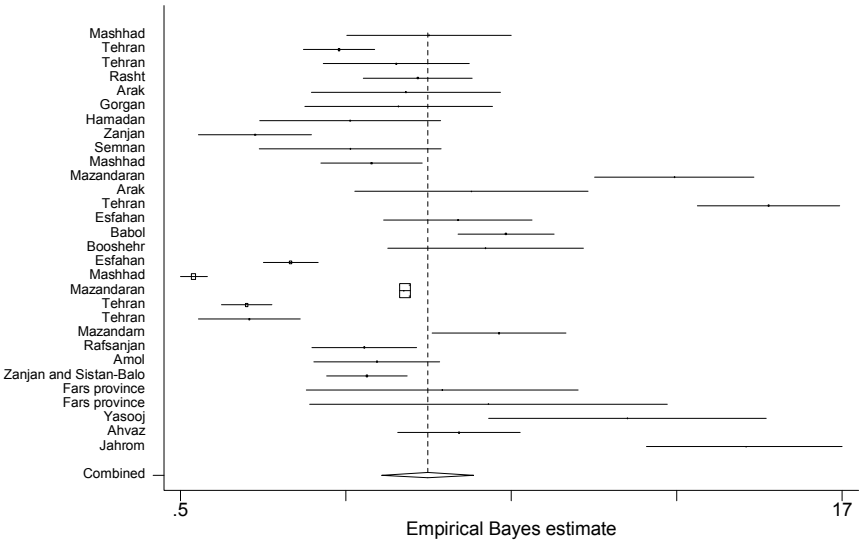

Figure 2. Difference the estimated prevalence of G6PD deficiency in each study and overall; this chart shows that the range in prevalence of G6PD deficiency in Iran is 0.8-15.2 (Based on Bayes analysis)

Table 3. Assessing the source of heterogeneity with Meta regression

Predictors	univariate		multivariate	
	coefficient	*P*-value	coefficient	*P*-value
Population study	0.7	0.4	-0.9	0.4
Site of study	0.3	0.03	0.4	0.03
Sampling blood	-1.7	0.1	-1.6	0.1

Discussion

This meta-analysis which was carried out with a systematic and structured strategy presented an estimation of prevalence of G6PD deficiency in Iran. Numerous studies with large sample size were examined in this research. This meta-analysis revealed that 6.7% of Iranians suffer from G6PD deficiency (that is, 5025000 people out of 75 million people in Iran). If it is ignored, they will face hemolytic crises and finally kernicterus (deafness, blindness, mental retardation, seizure and paralysis). In the present study, its deficiency in men was 4 times more than that in women; in different parts of Iran, its deficiency varied from 0.8 to 15.2 according to Bayesian analysis.

In a study by Eghbalian (16) on icteric infants in Tehran, prevalence of G6PD deficiency was 4.4%. Its prevalence in icteric children in Nigeria, India, Saudi Arabia, Singapore, Jamaica and Malaysia is 40, 12.2, 18.4, 1.62, 1.57 and 3.5% respectively (43-51); results of this meta-analysis (G6PD deficiency is 6.9% in icteric children) was less than some of these countries and more than others.

In a study carried out by Kosarian *et al*. (26) on 115622 infants in 3-7 days after birth using heel blood sampling, G6PD deficiency was 6.1%; ratio of boys to girls was 6.2%. It is higher than the results of the present meta-analysis on newborns. One of the probable reasons for this difference is that his study was conducted in Mazandaran (an area with high incidence), while the present meta-analysis considered a combination of all qualified studies in a broader areas including areas with both high and low frequencies. Padilla *et al*. reported

that incidence of G6PD deficiency in the Philippine was between 4.5% and 15.7; which matches the result of this meta-analysis.

Almost 7.5% of people in the world carry one or two G6PD deficient genes; its prevalence varies from 0.1% in Japan to 35% in Africa and some European countries (1). In reports presented before this meta-analysis, various levels of G6PD deficiency have been reported in Iran. According to WHO, prevalence of G6PD deficiency in Iran is between 10-14%; however, other studies reported the prevalence of 1 to 22.8% (1,5). In a meta-analysis conducted by Nkhoma *et al*. (9), total prevalence of G6PD deficiency in WHO regions including Africa, America, Asia, Europe, Middle East and Pacific, was 7.5, 3.4, 4.7, 3.9, 6 and 2.9% respectively; this figures were 8.5, 5.2, 5.2, 3.8, 7.2 and 3.4 respectively among males. Moreover, in a meta-analysis conducted by Nkhoma *et al*. (9), total prevalence of G6PD deficiency in the world was 4.9% (*i.e*. 329 million people suffer from this deficiency). In the present meta-analysis, the prevalence estimated for Iran is even more than its prevalence in eastern Mediterranean countries and Confidence interval of prevalence in Africa (which the highest prevalence) (7.1-7.9) overlaps the estimation presented in this meta-analysis (5.5-7.8).

Prevalence of G6PD deficiency for other groups (blood donors and male students, etc.) was much more than its total prevalence; the main reason was "gender" of the study population in these groups (approximately 90% of these people were male and its prevalence is 5 times more in men than in women.).

One of limitations of this meta-analysis was due to the place where the primary studies conducted in. These primary studies were carried out only in 60% of Iran regions with high prevalence of G6PD and the level estimated for the whole population is probably higher than the real level. Meanwhile, it was shown, in uni- and multi-variable analysis done to study the probable resources of heterogeneity, that study place was meaningfully the only heterogeneity factor among these studies. Various prevalence of G6PD in Iran is due to probable reasons like various ethnic groups such as Kurds in west, Arabs and Fars people in southwest and south, Balouch people in southeast and other populations in north of Iran as well as prevalence of malaria in the past (in different studies, a direct relationship was reported between G6PD deficiency and prevalence of Malaria), which has caused significant prevalence heterogeneity among different regions

According to Nkhoma *et al*. (9), Iran is among countries with high frequency and the observed difference in different parts of Iran is significant. Prevalence of G6PD deficiency in icteric newborns is more than that in normal newborns and other groups, but the observed difference among study population (icteric newborns, newborn, others) was not significant.

Although further similar studies regarding G6PD deficiency seems unnecessary, but, screening newborns on the day of birth plays an important role in informing families of such deficiency in their infants and to teach them how to protect their infants from being exposed to fava bean, Aspirin, sulphanamides and anti-malaria pharmacuticals, etc.

References

1. Farhud DD, Yazdanpanah L. Glucose-6-phosphate dehydrogenase (G6PD) Deficiency. Iranian J Publ Health 2008;37(4):1-18.
2. Iranpour R, Hashemipour R, Talaei SM, et al. Newborn screening for glucose-6-phosphate dehydrogenase deficiency in Isfahan, Iran: A quantitative assay. Arch Dis Child 2008;93(4):278-84.
3. Koosha A, Rafizadeh B. Evaluation of neonatal indirect hyperbilirubinaemia at Zanjan Province of Iran in 2001-2003: prevalence of glucose-6-phosphate dehydrogenase deficiency. Singapore Med J 2007;48(5):424-8.
4. Noori-Daloii MR, Soltanian S, Mohammad Gangi SH, et al. Molecular Identification of the Most Prevalent Mutations of Glucose-6-Phosphate Dehydrogenase (G6PD) Gene in deficient Patients in Khorasan Province of Iran. J Sci I. R. Iran 2006;17(2):103-6.
5. Noori-Daloii MR, Hajebrahimi Z, Najafi L, et al. A comprehensive study on the major mutations in glucose-6-phosphate dehydrogenase-deficient polymorphic variants identified in the coastal provinces of Caspian Sea in the north of Iran. Clin Biochem 2007;40(9-10):699-704.
6. Usanga EA, Ameen R. Glucose-6-phosphate dehydrogenase deficiency in Kuwait, Syria, Egypt, Iran, Jordan and Lebanon. Hum Hered 2000;50(3):158-61.
7. Haghdoost AA, Sadeghirad B, Hajarizadeh B, et al. The Application of Systematic Review and Meta-analysis Concepts in Summarizing the Findings of Observational Studies. Iran J Psychiatry 2007;2(4):132-6.
8. Nkhoma ET, Poole C, Vannappagari V, et al. The global prevalence of glucose-6-phosphate dehydrogenase deficiency: A systematic review and meta-analysis. Blood Cells Mol Dis 2009;42(3):267-78.
9. Yousefi J, Mirzadeh M, Malek A. The role of hemolysis in inducing jaundice in the newborns with G6PD deficiency, Iran J Pediatr 2006;16(4):461-6.

10. Hajiebrahimtehrani F, Faghihzadeh S, Borna H. The survey of necessary detection of Glucose-6-phosphate dehydrogenase in hyperbilirubinaemia newborn. Daneshvar Med 2004;11(51):29-32.
11. Hajiebrahim Tehrani F, Kholdi N, Fallah N, et al. Glucose-6-phosphate dehydrogenase (G6PD) Deficiency in icteric new born of inpatient, Daneshvar Med 2004;12(53):7-12.
12. Khalili D, Jafroodi M, Sajedi SA, et al. Survey of the prevalence of glucose-6-phosphate dehydrogenase deficiency in Rasht-Iran. J Gilan Univ Med Sci 2007;19(63):56-60.
13. Mojghan H. The prevalence of glucose-6-phosphate dehydrogenase deficiency in jaundiced newborn of Amirkabir hospitals of Arak in 2008 to 2009. J Rahavard Danesh 2000;3(1):33-8.
14. Ahmadpoorkachoo M, Mamoori G, Janaghi K. The prevalence of glucose-6-phosphate dehydrogenase deficiency in in hyperbilirubinaemia newborn. J Mashhad Med Facul 2001;44(71):91-5.
15. Eghbalian F, Monsef AR. Evaluation of Glucose-6-Phosphate Dehydrogenase Deficiency without Hemolysis in Icteric Newborns. Iran J Ped 2007;17(1):36-40.
16. Nobahar M, Vafaei AA. Investigation of glucose-6-phosphate dehydrogenase deficiency by NADP test in jaundiced newborn. J Qazvin Univ Med Sci 2004;29(1):46-51.
17. Boskabadi H, Omidian M, Mafinejad S. Prevalence and Clinical Manifestation of Glucose-6-Phosphate Dehydrogenase Deficiency in Newborns with Hyperbilirubinemia in Mashhad. Iran Maced J Med Sci 2010;3(1):1-5.
18. Ahmadi AH, Ghazizadeh Z. Evaluation of neonatal hyperbilirubinemia at Mazandaran Province of Iran in 2004-2007: prevalence of glucose-6-phosphate dehydrogenase deficiency. Res J Biol Sci 2008;3(8):934-9.
19. Sarreshtehdari M, Doulatshahi L. Determination of Glucose-6-phosphate dehydrogenase deficiency in icteric neonates. J Qazvin Univ Med Sci 2003;25(1):38-46.
20. Firoozrai M, Sedaghatkabli MR, Haghighi L. determination of frequency of Glucose-6-phosphate dehydrogenase(G6PD) deficiency in newborns with hyperbilirubinemia. JIUMS 2001;8(23):52-7.
21. Iranpour R, Akbar MR, Haghshenas I. Glucose-6-phosphate dehydrogenase deficiency in neonates. Indian J Pediatr 2003;70(11):855-7.
22. Zahedpasha Y, Ahmadpour M, Zahedpasha A. Glucose 6 phosphate Dehydrogenase (G6PD) deficiency. J Babol Univ Med Sci 2006;8(1):114-22.
23. Movahhed A, Farrokhi Sh. Incidence Rate of G6PD Deficiency in Newborns in Bushehr/Iran. Iranian J Pediatr 2003;13(1):55-8.
24. Mohammadzadeh A, Jafarzadeh M, Farhat AS, et al. Prevalence of glucose-6-phosphate dehydrogenase deficiency in neonates of Northeast of Iran. J Chin Clin Med 2009;4(8):448-51.
25. Kosaryan M, Nasehi MM, Karami H, et al. Neonatal Screening for G6PD Deficiency in Mazandaran Province, Iran 2007-2010. IJBC 2010;2(4):113-6.
26. Abolghasemi H, Mehrani H, Amid A. An update on the prevalence of glucose-6-phosphate dehydrogenase deficiency and neonatal jaundice in Tehran neonates. Clin Biochem 2004;37(3):241-4.
27. Khalesy N, Khosravi N, Haghighi M. Prevalence of Glucose - 6 - phosphate dehydrogenase deficiency in neonates born in Tehran-Iran (2008-09). J Gorgan Uni Med Sci 2012;14(1):100-5.
28. Mahdavi MR, Kosaryan M, Mortazavi A, Sangsefidi SH. The screening of G6PD deficiency in newborns of Sari, 1996. J Mazandaran Univ Med Sci 1997;8(2):22-4.
29. Alidalaki S, Negahban T, Halakooei M, et al. Investigation of Glucose-6-phosphate Dehydrogenase Deficiency in Rafsanjan, Autumn 2004. J Rafsenjan Univ Med Sci 2007;6(4):291-8.
30. Mortazavi Y, Esmaeilzadeh A, Kalantari S. Evaluation of molecular genetics of glucose-6- phosphate dehydrogenase deficiency and male individuals in zanjan city during 2001-2003. KAUMS J(FEYZ) 2006;9(4):1-6.
31. Hashemi SA, Zahed Pasha Y, Haji Ahmadi M, et al. Prevalence of G6PD deficiency among primary school students in Amol. J Babol Univ Med Sci 2005;7(1):52-6.
32. Mirzaei A, Fallahzadeh A, Haghbin S. Prevalence of Glucose-6-phosphate dehydrogenase deficiency in a student population in Yasuj. Armaghan Danesh 2000;5(17-18):63-7.
33. Mortazavi Y, Mirzamohammadi F, Teremahi Ardestani M, Mirimoghadam E, Vulliamy TJ. Glucose 6-phosphate dehydrogenase deficiency in Tehran, Zanjan and Sistan-Balouchestan provinces:prevalence and frequency of Mediterranean variant of G6PD. Iran J Biotechnol 2010;8(4):229-33.
34. Rahimi Z, Raygani AV, Siabani S, et al. Prevalence of glucose-6-phosphate dehydrogenase deficiency among schoolboys in Kermanshah, Islamic Republic of Iran. East Mediterr Health J 2008;14(4):978-9.
35. Mehrabani D, Pasalar M, Afrasiabi A, et al. Frequency of Thalassemia, Iron and Glucose-6Phosphate Dehydrogenase Deficiency among Turkish Migrating Nomad Children in Southern Iran. Acta Medica Iranica 2009;47(1):20-4.
36. Karimi M, Mehrabani D, Pasalar M, et al. Thalassemia, Iron and G6PD Deficiency in Lor Migrating Nomad Children, Southern Iran. IRCMJ 2010;12(4):441-5.

37. Nakhaee AR, Dabiri S, Noora M. Survey of the Prevalence of Glucose-6-Phosphate Dehydrogenase (G6PD) Deficiency in Admitted Men for Premarriage Tests in Zahedan-Iran Reference Laboratory. Zahedan J Res Med Sci 2009;11(3):33-40.
38. Nakhaee A, Salimi S, Zadehvakili A, et al. The Prevalence of Mediterranean Mutation of Glucose-6-Phosphate Dehydrogenase (G6PD) in Zahedan. Zahedan J Res Med Sci 2012;14(3):39-43.
39. Nabavizadeh SH, Anushiravani A. The prevalence of G6PD deficiency in blood transfusion recipients. Hematology 2007;12(1):85-8.
40. Amoozegar H, Mirshakeri M, Paishva N. Prevalence of Glucose-6-Phosphate Dehydrogenase Deficiency among Male Donors in Shiraz, Southern Iran. Iran J Med Sci 2005;30(2):94-6.
41. Kazemi Nezhad SR, Mashayekhi A, Khatami SR, et al. Prevalence and Molecular Identification of Mediterranean Glucose-6-Phosphate Dehydrogenase Deficiency in Khuzestan Province, Iran. Iranian J Publ Health 2009; 38(3):127-31.
42. Emamghorashi F, Hoshmand F, Mohtashamifar A. Screening for glucose-6-phosphate dehydrogenase deficiency in blood donors. Hematology 2010;15(2):122-4.
43. Ahmed H, Yulubu AM, Hendricks RG. Neonatal jaundice in Zaria, Nigeria- a second prospective study. West Afr J Med 1999;14(1):15-23.
44. Slusher TM, Vreman HJ, Melaren DW, et al. Glucose-6-phosphate dehydrogense deficiency and carboxy hemoglobin concentrations associated with bilirubin related morbidity and death in Nigerian infants. J Pediatr 1995;126(1):102-4.
45. Madan N, Sundaram K, Bhargava S. Glucose-6-phosphate dehydrogenase deficiency and neonatal hyperbilirubinemia. Indian J Med Res 1989;90:306-13.
46. Verma M, Singla D, Crawell S. Glucose -6-phosphate dehydrogenase deficiency in neontes, prospective study. Indian J pediatr 1999;67(9);386-9.
47. Yaish HM, Niazi GA, al Shaatan M, et al. Increased incidence of hyperbilirobinemia in 'unchallenged' glucose-6-phosphate dehydrogenase deficiency in term Saudi newborns. Ann Trop Pediatr 1991;11(3):259-66.
48. Joseph R, Ho LY, Gomez JM, et al. Mass newborn screening for glucose-6-phosphate dehydrogenase deficiency in Singapore. Southeast Asian J Trop Med Public Health 1999:30(suppl 2):70-1.
49. Gibbs WN, Gray R, Lowry M. G6PD deficiency and neonatal jaundice in Jamaica. Br J Hematol 1979;43(2):263-74.
50. Hon A, Balakrishnan S. Hyperbilirubinemia and erythrocyte Glucose-6- phosphate dehydrogenase deficiency in Malaysian newborns. Med J Malaysia 1998; 44(1): 30-4.
51. Padilla C, Nishiyama K, Shirakawa T, et al. Screening for glucose -6-phosphate dehydrogenase deficiency using a modified formazan method: a pilot study on Filipino male newborns. Pediatr Int 2003;45(1):10-5.