Research Article

Genetic Screening for Nicotine Dependence and Treatment Approaches among Physicians in Indonesia

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ABSTRACT

This study is the first to query Indonesian physicians about medical genetics in detail for smoking cessation and smoking-related diseases from health care sites in multiple cities across Indonesia. 113 physicians completed a survey questionnaire assessing their opinions on genetic screening use for smoking cessation and smoking-related diseases, medical genetic facilities available to them, and information from medical genetics that are of interest. Pearson's chi-squared or Fisher's exact tests were applied to evaluate associations between genetic screening usefulness with institutional affiliation, clinical specialty, and research interest. 81% of total respondents indicated that genetic screening information for smoking cessation would be useful. 56% of the physicians were based in a clinic and 63% were general practitioners. Most research interests were in respiratory diseases (35%) and nicotine addiction (28%). Institutional affiliation was significantly associated with opinions on usefulness ($p = 0.018$) as was an interest in cancer pathology ($p = 0.005$). 42% of physicians believed they lack the knowledge on what specific information would be useful but 70% still believe genetic screening would be useful. 89% of physicians stated that their affiliated institutions had limited medical genetics services and facilities. This report found an optimistic interest in genetic screening for smoking cessation and related diseases among Indonesian physicians despite limited resources for immediate incorporation of genetic screening information into their practices.

Keywords: Smoking cessation, tobacco use disorder, genetic testing, Indonesia, physicians.

INTRODUCTION

The act of smoking is deeply ingrained in the Indonesian people's daily lives and social culture. Indonesia is the fourth highest cigarette consumer in the world after China, Russia, and USA[1]. As of 2011, approximately 60 million people in Indonesia smoke cigarettes on a daily basis with an average daily cigarette consumption of 12-13 sticks[2]. Indonesia is one of the few countries in the world with much higher rates of smoking in males (57%) than females (under 4%)[1]. Smoking initiation typically begins around the ages of 17-18 with almost 13% of smokers beginning before the age of 15[2].

Smoking cessation remains to be the most effective way to reduce the impacts of tobacco consumption. The effects of smoking cessation materialize much more rapidly than the damaging effects of smoking. Additionally, individuals who began smoking at an early age yet stopped smoking before the age of 40 has a 90% higher likelihood of avoiding tobacco-attributed diseases[3]. A recent survey of Indonesian smokers discovered relatively low interest in quitting (only 48% compared to 70% for countries such as United States and United Kingdom)[4, 5]. The small percentage of Indonesian smokers who did quit, achieved it through no aid whatsoever, which further contributes to the difficulty of smoking cessation in the nation[2].

A vital basis for low success rates in quitting smoking without aid is nicotine's stronghold on brain physiology. Pharmacotherapy is the most effective method to deal with withdrawal symptoms caused by neurochemical responses to nicotine absence, thereby increasing the chance for long-term cessation by 50-70%. This is particularly true for smokers who consume between 10-15 cigarettes per day[6]. A well-established biological basis to nicotine dependence is found in genetics, particularly in variations of the hepatic cytochrome P450 2A6 (CYP2A6) and nicotinic receptors (CHRNA) genes. The CHRNA gene family is involved in smoking-behavior patterns (e.g. smoking heaviness, time to first cigarette per day) through its relation to the neurological reward system from nicotine intake[7]. Nicotine metabolism and clearance by the liver is heavily influenced by CYP2A6 gene variation; these variants could also be useful in determining an individual's likelihood in lung cancer development due to smoking[8]. Moreover, genes relevant to nicotine dependence and metabolism have been found to be essential in determining the efficacy of different pharmacotherapy methods as well as in predicting risk of smoking relapse[9].

Genetic screening and notification have the potential to advance patient treatment[10]. Since genetic variation impacts nicotine metabolism, smoking behavior, and a cessation method's efficacy, it becomes a significant puzzle in research and for physicians to recommend the best approach for a patient wanting to quit. Within the context of smoking cessation, genetic screening information has been shown to increase cessation success rate and improve cessation interest through heightened patient health awareness[11]. Several FDA-approved drugs

in the United States are available for smoking cessation such as varenicline and bupropion. However, physicians are cautious about prescribing them due to potential adverse, psychiatric side effects. The nicotine metabolite ratio (NMR), which is heavily influenced by CYP2A6 gene variants, has shown promise as a biomarker to optimize pharmacotherapy assignments by improving efficacy and reducing side effects. From a medical practice standpoint, this means that physicians could be assigning nicotine dependence treatments to their patients based on a blood test to assess their NMR profile in the near future[11]. While these findings are particularly encouraging, there are barriers to using the NMR in practice. Physicians may still misunderstand available treatment approaches, genetic screening's role and limitation, and proper ways to interpret and deliver results to patients[12].

Policy-based interventions in tobacco-product use in Indonesia are limited, largely non-governmental supported, and are subject to legal interferences by tobacco companies[13]. A strong symbol of this is Indonesia's status as the only Southeast Asian nation yet to sign the WHO Framework Convention on Tobacco Control Treaty[2], which implementation has proven to be an effective way of reducing tobacco consumption[3, 13]. Several investigations that are part of the Quit Tobacco International Project based in the province of Yogyakarta find that 75% of the physicians have a lax attitude about asking patients about their smoking habits. 20% of the surveyed physicians (particularly male) are smokers themselves while 80% of the physicians believe that smoking up to 10 cigarettes per day does not harm a person's health[2,14]. However, these studies tend to be in a single site and have comparatively small samples. Given that the health care providers are a part of the nation-wide public health problem, it is important to assess their interest in improving care for smoking cessation and smoking-related diseases at multiple cities and institutions. One tool that is under-utilized in Indonesia is medical genetics, which ties in strongly with pharmacotherapy and its selection to improve efficacy through physician advice.

The appropriate pharmacotherapy cessation aid can significantly impact an individual's success at quitting smoking, thereby placing a vital role on physicians. Due to the lack of official reports on genetic screening interest for smoking cessation in Indonesia, this study first investigates physicians' interest in using genetic-based screening within the context of smoking cessation consultation. The study also looks at the Indonesian health care providers' interest in information on smoking-related diseases as well as physicians' current access to medical genetics for their medical practices.

MATERIALS AND METHODS

This study was funded by Bina Nusantara University to evaluate physician interest in genetic technologies and screening programs. Questionnaires were the primary data collection instrument. The physician questionnaire consisted of 12 questions, surveying participants on: medical specialty, health care facility affiliation, patient population profile, medical research interest, opinion on genetic screening technology, and medical genetics tools accessibility.

Purposive sampling led to the participation of physicians from several urban cities across Indonesia, including the greater Jakarta metropolitan area, Bandung (West Java), Semarang (Central Java), Yogyakarta, Malang (East Java), Palembang (South Sumatra), and Makassar (South Sulawesi). All 113 health care professionals responded to a hard-copy questionnaire in-person and completed the questionnaire at the site of their health care facility posts during their own time. The survey targeted physicians with interests in respiratory diseases, nicotine addiction, and cancer pathology since they were assumed to have higher interest in smoking cessation and smoking-related diseases. The responses were entered into a MySQL database by trained data entry staff[15]. All statistical analyses were performed on [R], particularly Pearson's chi-squared test or Fisher's exact test to quantify associations between opinions of genetic screening usefulness and physicians' profile[16]. Associations with usefulness were tested for each profile category (organization type, medical specialty, research interest). For organization type and research interest, each individual item's association with usefulness was assessed as well. P-values less than 0.05 were interpreted as statistically significant associations.

RESULTS

113 surveys were collected and Table 1 summarizes the physician survey's results. Most of the physicians surveyed were affiliated with a clinic (56%). 63% of the physicians were general practitioners, reflecting the predominant affiliation to clinics. The most dominant research interests were respiratory diseases (35%) and nicotine addiction (28%).

Overall, 81% (n = 89) of total respondents indicated that genetic screening information for smoking cessation would be useful. Institutional affiliation and usefulness have a statistically significant association ($p = 0.018$). Individual categories for research interest were tested only independently against usefulness since a physician could select more than one research interest. The usefulness rating was significantly associated for interest in cancer pathology ($p = 0.005$) and in other research fields (grouping among 13 categories written-in by the physicians; $p = 0.003$). Usefulness was not significantly associated with interest in respiratory disease and nicotine addiction ($p = 0.06$ and 0.074 respectively). Medical specialty was not significantly associated with usefulness ratings ($p = 0.222$).

Table 1: Profile of surveyed physicians

		Genetic Screening Usefulness for Smoking Cessation N (%)[1]			
	Total N(%)[1]	**Very Useful**	**Somewhat Useful**	**Not Useful**	**p-value**
Institutional Affiliation					
Hospital	48 (44)	21 (45)	22 (48)	3 (7)	0.018
Clinic	62 (56)	16 (26)	30 (49)	15 (25)	0.043
Medical Specialty					
General Practitioner	71 (63)	19 (28)	38 (55)	12 (17)	0.108
Non-GP	42 (37)	18 (44)	17(41)	6(15)	0.222
Medical Research Interest					
Respiratory Diseases	40 (35)	17 (47)	12 (33)	7 (19)	0.060
Cardiovascular Diseases	19 (17)	8 (42)	6 (32)	5 (26)	0.423
Cancer Pathology	9 (8)	7 (78)	2 (12)	0 (0)	0.005
Nicotine Addiction	32 (28)	15 (47)	15 (47)	2 (6)	0.074
Substance Abuse/Addiction	7 (6)	1 (14)	5 (72)	1 (14)	0.423
Others[1]	34 (30)	5 (15)	20 (59)	9 (26)	0.003

[1]Categories with less than 5 observations were not included in analysis or grouped together as 'Others' for analysis

Table 2 summarizes the physicians' expected and current experience with genetic screening. The survey found that 42% of physicians were interested in genetic information on respiratory, cardiac, and psychiatric diseases. 23% were interested in genetic information on addiction. 42% of physicians believed that they did not have enough knowledge to decide what type of information from genetic screening would be useful. Nonetheless, 70% of those who deemed themselves to lack knowledge stated that genetic screening information would be useful at some level for smoking cessation. 89% of physicians stated that their affiliated institutions were limited in medical genetics services and facilities.

In addition to questions yielding the results in Table 1 and 2, the survey also included a question that asked physicians to report the percentage proportion of their patients who are current smokers. 27% (N = 30) of the surveyed physicians could not provide a response to this question. Based on the physicians who did respond to the question (N = 83; 73%), it was found that smokers, on average, comprise 45% of a physician's patient list.

DISCUSSION

A 2011 survey performed by the World Health Organization (WHO) on Indonesian smokers finds that only two-thirds of the surveyed patients recalled ever having a physician ask them about their smoking status[2, 14]. Our study complemented this finding with 27% of the surveyed physicians not knowing how many smokers they were currently treating. The lack of knowledge on patient smoking status is worrisome since proactive health care providers play a crucial role in smoking cessation success. Physicians are recommended to practice the 5 A's in smoking cessation counseling: Ask, Advise, Assess, Arrange, and (re-) Assess[17]. It is also important for physicians to understand how to interpret genetic screening results and effectively relay the findings to patients[18]. This is especially true given major concerns that primary care physicians and general practitioners have over the sensitivity and complexity of medical genetics information[19].

Despite the relatively low interest in patient smoking status and limited resources for genetic screening available to Indonesian physicians, we found a positive response towards medical genetics for smoking cessation. Even 70% of those who did not know what type of information they would like from genetic screening stated that having it as a medical practice tool would be useful for at least smoking cessation. This is promising because 56% of the physicians surveyed were based in clinics. Compulsory community clinics remain the most affordable and most widely-visited form of health care for the Indonesian population, making these clinics the most far-reaching source of information on smoking cessation and smoking-related diseases[20].

Table 2: Indonesian physician and genetic screening

Existing Medical Genetics and Related Services (n = 113)	N	%
Genotyping	9	8
Sequencing	3	3
None - institution limited in this area	101	89
Genetic Screening Information Interest (n = 113)		
Genome-wide analysis	9	8
Addiction-related gene screening	26	23
Pharmacogenetics	22	19
Respiratory, cardiac, psychiatric diseases screening	48	42
I don't know - better leave decision to experts	47	42
Genetic Screening Usefulness of 'I don't know' Responders for Smoking Cessation		
Very Useful	11	23
Somewhat Useful	22	47
Not Useful	14	30

One setback in the survey collection was the oversight of not interviewing the physicians in-person. The logic to this was to respect the privacy of the physicians by having them complete the questionnaires at their own time. However, this led to some missing values to the questionnaires. The survey also did not have a direct question to gauge how comfortable physicians would be in implementing or incorporating genetic screening information into their daily medical practices if the tools became available to them, taking upon the role of a provider and interpreter of medical genetics information.

Physician opinion is one side of the story when it comes to smoking cessation efforts on a public health scale. Opinions and attitudes of patients are also crucial pieces of the puzzle. Therefore, the next step to our research is to survey smokers' opinion on genetic screening for smoking cessation.

We observed an optimistic and promising interest in genetic screening among Indonesian physicians for smoking cessation and related diseases despite limitations in the availability of medical genetics facilities. Most physicians who stated that they lack the proper knowledge to specify information they wish to gain from genetic screening still believe that the tool would be useful for smoking cessation consultation and nicotine dependence treatment. Therefore, education on information use and interpretation, facility and technology availability, and most likely monetary costs would be barriers in efforts to implement genetic screening for smoking cessation consultation in Indonesia.

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