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Peking University Centennial Memorial Hall

Peking University Centennial Memorial Hall was built to celebrate the 100th anniversary of the founding of Peking University. The architecture design of the Memorial Hall is delicate and solemn, with impressive feelings of texture and vivid feature of era. It is harmonically refl ected the understanding and succeeding of the history and spirit of Peking University. Peking University Centennial Memorial Hall now becomes another landmark of Peking University.

(*Photo by Xin Zhao*)

News

China's efforts at avian influenza treatment and prevention

Jinpei Li[1], Ruifang Fan[1], Yonggang Li[2], Xun Li[2,*]

Keywords: Avian influenza virus, H5N1, Treatment and prevention, China

In recent years, an unprecedented epizootic avian influenza virus, known as A (H5N1), that is highly pathogenic has crossed the species barrier in Asia to cause many human fatalities and an increasing pandemic threat from Southeast Asian to other countries, with occasional transmission to humans (*Enserink M. Science. 2009; 323:324*). According to the latest statistics from the *Hongkong Government Information Center*, as of January 19, 2009, 393 human cases of positivity for H5N1 involving 248 deaths have been reported from 2003 to 2009 (*http://www.info.gov.hk/info/flu/eng/global.htm*).

H5N1 virus, an influenza A virus subtype that occurs mainly in birds, is highly contagious among birds and can be fatal to them. At present, despite the detected cases of infection with the influenza A virus, human-to-human transmission is rare (*Beigel JH, Farrar J, Han AM, et al. N Engl J Med. 2005; 353:1374-1385*). However, given the extreme variability of this kind of virus, together with the fact that humans have no natural immunity to it, there is great concern about the possibility of a new mutational virus subtype or reassortment of the current avian influenza virus with a pandemic potential.

To date, the pathogenesis of human transmission is still not clear; as a consequence, despite considerable knowledge about viral infectivity current antiviral treatment and therapeutic measures cannot control this disease. All in all, the apparent lethality of H5N1, combined with its inexorable spread, are what have led scientists worldwide to take it seriously.

China is one country where these issues are a major concern. According to Xinhua News, as of January 19, 2009, there have been 4 cases in which 3 people died of the H5N1 virus, and the latest involves a woman from Ji'nan who died on January 19th (*http://news.china.com/zh_cn/domestic/945/20090121/15292507.html, available as of January 21, 2009*).

From a geographical point of view, China is located along the main migratory routes of birds, and migratory birds have become essential carriers and disseminators of avian flu. Additionally, China has large numbers of poultry and a large population, providing more chances for transmission, including bird-to-bird, bird-to-human, and even potentially human-to-human transmission. As a result, since the first case of human infection was detected in Hong Kong, the public has welcomed a series of measures that have been taken by Chinese authorities to provide effective avian influenza treatment and prevention, which are summarized in the following.

First, extensive dissemination of knowledge related to H5N1 has taken place to eliminate public stress and to raise awareness of hygiene and safety and encourage self-vaccination. Moreover, a medical monitoring system and network laboratories have been established to improve and standardize infection detection, reporting, quarantine, and treatment and to facilitate communication with the WHO Global Influenza Surveillance Network.

Second, institutions handling epidemics and animal disposal should be provided in order to decisively handle and promptly announce any epidemics. For instance, in areas where a pathogen is suspected or that have been affected by disease, primary measures have concentrated on inoculation, compulsory vaccination, and proper disposal of carcasses and animal waste, and especially contaminated manure, with the exception of eradicating all natural reservoirs within 3 kilometers of the area. In other areas and especially those with poultry farms or processing plants, vaccination or disinfection is performed using ultraviolet radiation or chemical disinfectants.

Third, import and export inspection and quarantine have been enhanced to prevent incoming and outgoing epidemics. At the same time, the government has implemented stricter trafficking laws and regulations and imposed severer and harsher penalties on the smuggling of poultry products.

Fourth, but not last, the government has increased funding of scientific research to develop effective vaccination or anti-influenza agents as soon as possible. The PRC is currently forming noted scientific teams from both clinical and research institutes to study the mechanisms for H5N1 infection in terms of aspects such as virus mutations, circulation, and cross-infection

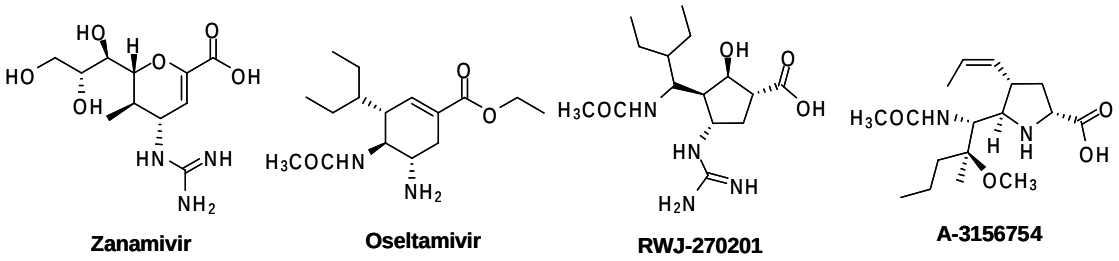

Figure 1. Four NA-based antiviral agents.

between animals and humans.

Given these efforts, however, vaccination provides limited control because of the tendency of the virus to mutate, allowing it to evade the immune system. Thus, vaccines must be reformulated each year due to high antigenic drift (*Sun S, Cui Z, Wang J, et al. Avian Pathol. 2009; 38:31-34*). Thus, effective naturally available or chemically synthesized anti-influenza therapeutics represent an urgent need at present.

Early options for the therapeutic treatment of influenza are Amantadine and Rimantadine, which act by interfering with the M2 protein ion channel that is found only in influenza virus A. However, the clinical use of these agents is limited both because of their insensitivity to influenza virus B as well as to the rapid emergence of resistance (*Heins JR, Plamp J. S D J Med. 2004; 57:529-531*).

Recently, neuraminidase (NA) inhibitors have quickly developed as anti-influenza agents because NA is crucial to the release of virion progeny by infected cells as well as its important role in the replication and movement of the virus through the mucus of the respiratory tract and because these inhibitors can reduce the propensity of the virus particles to aggregate (*Liu C, Eichelberger MC, Compans RW, Air GM. J Virol. 1995; 69:1099-1106*).

The most famous NA-based inhibitors of influenza, Relenza (Zanamivir-ZMV by Glaxo Wellcome/Biota) and Tamiflu (Oseltamivir-OMV by Hoffman-La Roche/Gilead), have been confirmed as effective and safe for the treatment of influenza and both have been approved by the US FDA. Additionally, two other NA inhibitors, RWJ-270201 (BCX-1812) and A-315675, are undergoing phase III trails in North America and Europe (*Young D, Fowler C, Bush K. Philos Trans R Soc Lond B Biol Sci. 2001; 356:1905-1913*), respectively; the two are shown in Figure 1.

In China, a series of measures have been taken by authorities to support the development of effective anti-influenza agents. As early as 2005, for instance, after the outbreak of highly pathogenic avian influenza an "Emergency research project regarding anti-influenza agents" was undertaken by the Shanghai Institute of Materia Medica (SIMM) (*http://www.simm.ac.cn/news/200812179035.htm, available as of December 17, 2008*). Led by professors Jiang Hualiang and Shen Jingkang from SIMM, the scientific research group consists of three units, the SIMM, Nanjing Simcere Dongyuan Pharmaceutical Co., Ltd., and Nanjing EffactPharm Drug Development Corp.

Thanks to their efforts, conditions for the synthesis and corresponding capsule preparation of Zanamivir were accomplished, and imitation and "me-too" drugs were developed at the same time. Zanamivir was approved by the Chinese State Food & Drug Administration (SFDA) for clinical testing on November 7, 2008 (Permit No 2008L09511).

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Original Article

Assessment of the experiences and coping strategies of people working in the informal sector in their quest to access health care services: The case of Dar es Salaam, Tanzania

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Summary **Addressing inequities in health care provision and financing has been at the center stage of Health Sector Reform (HSR) discussions since the early 1980s. The poor, women, and informal health sector workers in most developing countries are rarely covered by formal health insurance mechanisms that are meant to ensure access to essential health services. They are also sidelined in formal banking and credit systems due to their being predominantly low income earners, with little resources to meet eligibility criteria for borrowing and also to be considered creditworthy. In light of this fact, the present paper analyzes both quantitative and qualitative data in an attempt to explore and discuss the experiences and coping strategies of women and men employed in the informal sector economy in their daily attempts to access health care services. The paper employs Malaria as a tracer disease and gender as a unit of analysis. Analysis indicated the significance, as perceived by interviewees, of both informal credit networks and formal insurance and banking systems as important shock-absorbers for vulnerable populations in their struggle to access basic health services in times of need. The paper further highlights and discusses diverse coping strategies that households employ in dealing with illness-related costs and a greater willingness to be integrated into both formal and informal financial mechanisms. The paper finally concludes that the government must take the following steps: 1) enhance existing formal and community-based initiatives to make them sustainable, 2) devise ways to reduce the lack of flexibility in membership requirements for insurance schemes/financial institutions, and 3) reduce perverse incentives inherent in the health system that may prevent people from seeking membership in available insurance mechanisms. In addition, deliberate steps must be taken by the government to employ 'targeted measures' to ensure that health care access is improved and sustained particularly for vulnerable populations.**

Keywords: Informal sector, (In)Equity, Coping strategies, Access, Malaria

1. Introduction

1.1. *Background*

Addressing inequities in health care provision and financing has been at the center stage of Health Sector Reform (HSR) discussions since the early 1980s. More specifically, increasing access to health care for vulnerable African populations is one of the formidable challenges facing the global community (*1*). During the 1980s and 1990s, HSR intended to improve the efficiency of health systems in terms of delivery and financing of health services. A noble goal of these reforms was, among others, improve health care access for the poor and vulnerable populations who were already shouldering a dual burden of poverty and ill health.

In many countries (including Tanzania), these reforms included the introduction or consolidation of cost recovery mechanisms (in particular, out-of-pocket fees paid in the event of illness) which unfortunately had had an unintended consequence of decreasing access to health care for vulnerable population such as

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poor women and men (*1-3*).

Studies in most African countries have established that, in the event of ill health, poor households do not have recourse to mechanisms that will protect the financial resources for basic consumption needs such as transportation, education, health, and food not produced by the household (*1*).

Studies have further shown that even when mutual health insurance exists, low income households are initially reluctant to join insurance schemes because they do not readily accept the idea of paying for services they might not use (*4*).

Both in developing and developed countries issues of gender inequities in health have been "broadly" addressed to the extent that there are still some health equity gaps existing not only between men and women but also between and among women employed in the formal (modern sector) and those employed in the informal sector.

Given the historical fact that women in low income countries are the most disadvantaged in terms of bearing a higher burden of disease and being poorly covered by formal social security arrangements, there is an emerging consensus that, more than men, they should be given a higher priority and covered under existing social security schemes for health risks as workers and in their gender roles as mothers and widows. On both counts, however, coverage for women is often unsatisfactory. In many cases women remain invisible as independent workers in social security schemes (*5*).

Given the ongoing economic reforms and especially the privatization of public enterprises, most women have found themselves outside formal sector employment as a result of entrenchment. Problems of access as an important component of equity are even more entrenched and marked among women who are not employed either in the formal or in the informal sector.

There have been several efforts by health systems both in high and low income countries to institute support systems intended to ensure financial security necessary to bear the costs of access to health care services. Among the noted approaches employed by many countries, including Tanzania, is the establishment of National Health Insurance Funds (NHIF) and Community Health Funds (CHF).

One must acknowledge, however, that even in places where there are community health funds, not all women are members. Moreover, the fact that the NHIF (in Tanzania, it unfortunately has not covered all formal sector employees, much less those in the informal sector) excludes the unemployed leads to the conclusion that a significant number of women will be marginalized as they will not be directly or indirectly benefiting from the fund. This conclusion is based on the fact that in Tanzania proportionally fewer women are employed in the formal sector than men (*6*), a phenomenon that may potentially perpetuate their exclusion from formal financial security systems aimed at improving health service access and utilization as well as general socioeconomic wellbeing.

In Tanzania, like in most other developing countries, access is virtually restricted to few people who can afford to pay the associated costs of health care in the time of need. Research and experience has demonstrated that there is no sustainable health insurance for the rest of the population, most of which is often poorer than the salaried workers of the public and private sectors (*3*).

According to Letourny (*7*), illnesses such as malaria are unpredictable and occur randomly, their consequences are fatal and in most cases lead to loss of household income and increased household expenditures despite limited household resources. Unfortunately, solutions to cope with these illness-related costs are limited because among informal sector employees there is a significant reliance on traditional solidarity mechanisms that are inadequate and not sufficiently sustainable to cover the costs of health and economic risks with a reasonable degree of certainty (*3*).

While limitations of access to health care services may be even worse among the unemployed (than any other group in the formal or informal sectors), the current study refers strictly to people employed in the informal sector for both reasons of scope and reasons related to the potential role that the informal sector is likely to play to improving the country's economy in general and socioeconomic development for the poor in particular.

Moreover, the traditional notions of family with men as the primary breadwinner and head of households and women as dependants is often applied in the implementation of social security and social assistance schemes, including those related to health risk protection (*8*). Another important problem exists and is related to the fact that most women who work are in casual employment, with the result that they have to build up a certain contribution history before they are covered again by the scheme of their new employer (*5*), if they are somehow employed in the formal sector. This places women outside the margins of any existing form of social and protection mechanisms.

In addition, the rationale to emphasizing the study of informal sector employees in a low income setting like Tanzania is based on evidence from studies such as that conducted by Aday and Anderson (*9*), who demonstrated that there is a close relationship between access costs and utilization of health care. Access costs are influenced by factors such as waiting time at the facility and out-of-pocket payments, all of which may impact not only utilization but also the effectiveness of the health program (*10*). Thus, being predominantly low income earners…., there is a good reason to study informal sector workers who are, as explained in the current study, a vulnerable population because they face potential challenges in their attempt to access health care services due to their predominantly low incomes.

Access barriers to health care utilization are diverse.

However, health care costs constitute the major bulk of barriers to financial security for vulnerable groups such as women in the informal sector economy and thus represent a critical policy challenge. In essence, the existence of sustainable financial security mechanisms that can be accessed by all people, including the poor, can facilitate the softening of the effects of some factors that represent potential barriers to health care access, efficient and effective utilization of health care services, and ultimately improved health as the central policy goal of all health systems.

Uncertainty about the timing of illness (like malaria), unpredictability of health care costs during illness, and the low and irregular income of individuals (*1*) such as women and men in the informal economy make it virtually impossible for households to make financial provision for illness-related expenditures. Furthermore, most households with lives tied to informal sector activities are unable to obtain credit from formal banking systems, a phenomenon which makes them even further marginalized. In a nutshell, inadequate financing of health services in low income countries such as Tanzania and the absence of universal coverage leaves most informal sector employees in medical indigence as they cannot bear the unpredictable financial consequences of ill health.

Against this background, the current study attempted to achieve the following objectives. To generally assess the experiences of people in the informal sector in their quest for health care services, the problems and barriers they face, and the steps they take to deal with these problems. Specifically, the study compares rural and urban residents and women and men working in the informal sector in terms of their experiences, problems, and steps they take to cope with the realities of seeking and gaining access to health care services. Importantly and from a gender perspective, the paper explores and describes the associations between socioeconomic and cultural characteristics of individuals employed in the informal sector and their experiences and coping strategies in relation to barriers to health care access.

The rest of the paper is organized as follows. Section 2 sketches a conceptual framework under which the definitions of informal sector employees are described from a broader global view, and a particular context is presented to reflect the situation in Tanzania. Section 3 describes the methodology employed in the paper. Results are presented in Section 4. Section 5 interprets and discusses the main findings in relation to their policy implications and, finally, conclusions are presented in section 6.

1.2. *Different forms of informal sector employees*

Social security for the formal sector has traditionally involved coverage of formal sector workers (and their dependants) because of their ability to contribute to their own insurance from their salary. Also covered are workers who have informal labor relations with their employers, which often means the absence of written labor contracts (*11*).

Such informality does not only affect wage-earners and other groups such as home workers in the informal sector, but also casual workers who work – directly or indirectly – for formal sector enterprises. Some populations, such as widows, orphans, and the elderly, are neither protected by the salary of the breadwinner nor by any other family protection; these groups must be protected by tax-based social assistance (*11*).

In principle and according to the International Labor Organization (ILO) (*11*), informal sector workers are employed in a (micro-) enterprise that has the following characteristics: the owner is personally liable for gains and losses (the enterprise is unincorporated); absence of full and written accounts; and the enterprise has fewer than ten continuous employees. Apart from informal enterprises, there are also informal labor-relations, signifying the absence of written labor contracts. All of these informal (sector) workers have very different employment conditions that have a direct impact on their social health security needs and on how they organize security support systems for themselves. According to the ILO (*11*), the main characteristics for the ideal types would entail the following:

Urban/rural. Urban informal workers tend to be more heterogeneous, so establishing associations for social security purposes (*e.g.* health) is more difficult. Urban workers tend to be more interested in housing than workers in rural areas, where space is more plentiful and building materials directly available. In such instances, rural informal sector workers (*e.g.* women) are considered to be much more interested in health issues than housing given the fact that in most developing countries health sector infrastructures in rural areas are often worse than in urban areas.

Self-employed/wage-earner. Self-employed workers are relatively better off and better organized than wage-earners, with the result that they are better candidates for successfully organizing financial and social security (including those related to health risk protection) for themselves in cooperatives or other producer organizations.

Resident/transient. Where people are working and living in a fixed place, they are more likely to build up the necessary trust to set up a social security scheme amongst themselves. Therefore, people working in the street economy of urban areas or circular migrants in rural areas are unlikely to be covered by social security.

Regular/casual. Most regular workers in the formal sector are covered by compulsory social insurance

schemes, but because of non-compliance many regular workers are not covered. Casual workers both in the formal and informal sectors have little chance of being protected by compulsory or voluntary social insurance schemes.

1.3. *Definition of the informal sector: A Tanzanian perspective*

According to the Integrated Labour Force Survey of 2000/2001 (*6*), the informal sector is considered a subset of household enterprises or unincorporated enterprises owned by households. Characteristically, the informal sector entails enterprises that are not separate legal entities, independent of the households or household members who own them. These enterprises do not have a complete set of accounts as would permit a clear distinction of production activities of the enterprises from other activities of their owners. Moreover, the identification of flows of income and capital between enterprises and owners of the enterprises may or may not involve paid labor, and activities may be carried out inside or outside the owners' home, where some of the goods or services of the business must originate. In the current study, this definition and the ILO's (*11*) conceptual forms of informal sector employees are used.

In Tanzania, the informal sector is increasingly becoming an important employer given new challenges posed by ongoing economic, social, and political reforms (*6,12*). Nationally, about 36% of male-headed households are involved in the informal sector economy, as compared to 32% of female-headed households (*6*). Although female employees constitute a significant but relatively small proportion in comparison to men in the informal sector, they more often than not find themselves in a peculiar state of vulnerability resulting from their social position in society, often exposing them to difficulties and poor access to health care services.

2. Methods

2.1. *Study design and sites*

This was a cross-sectional study conducted in four wards of Ilala District in the Dar es Salaam region between August 2005 and January 2006. Dar es Salaam was chosen because it has the highest proportion of households employed in the informal sector economy. According to the Integrated Labour Force Survey 2000/2001 (*6*), about 62% of households in Dar es Salaam are engaged in informal sector activities of one form or another.

2.2. *Stratification and sampling*

A multi-stage sampling procedure was used. The first stage involved purposeful selection of one district (Ilala district), followed by a stratified random sampling of four wards, two with urban characteristics and another two with rural characteristics. The third stage involved randomly selecting four villages/areas, one from each stratified ward. Since certain parts of the study share both rural and urban characteristics (semi rural/semi urban), geographical ward[1] boundaries were used to identify and locate appropriate study areas. This exercise was done in consultation with relevant authorities. The technique (Multistage sampling) was employed so as to ensure sampling efficiency and representativeness.

2.3. *Data collection techniques and tools*

This study used both qualitative and quantitative research methods. Qualitative techniques were used given their philosophical roots, which emphasize the importance of understanding social and cultural processes in shaping human behavior (*13*). The technique involved Focus Group Discussions (FGDs). The Swahili language was used for discussions, as it is common in the study areas. A quantitative method was implemented through administration of a structured questionnaire with close-ended questions. In consultation with key informants, participants were drawn from groups of men and women who are employed in informal sector activities. At the end of the study, 368 participants consented to be included in questionnaire interviews.

2.4. *Structured interviews*

Interviews were administered at the household level in consultation with community leaders (key informants) to help interviewers identify respondents who were specifically in the informal sector economy. The same mechanism was applied to determine participants for focus group discussions.

2.5. *Focus group discussions (FGDs)*

Focus group discussion sessions were conducted with groups of women and men who were employed in the informal sector economy. Discussions were intended to solicit views on experiences in terms of health care access, financial problems faced in attempts to access health care services, and strategies employed to cope with these problems. Both audio-taping and note-taking were used to collect information.

[1] A 'ward' is an administrative unit below a 'division'. The district is the highest administrative structure and its geographical coverage comprises a number of divisions and wards. Below wards are villages and 'hamlets'. A 'hamlet' is the lowest unit in the local government administrative structure.

In collaboration with key informants at the community level, FGD participants were purposely selected on the basis of their participation in the informal sector economy, their shared experiences and interests, knowledge of the subject under investigation, and willingness to participate in the discussions (*14*). A key informant was considered to be a member of the study population who offered to inform or educate the researcher on a given subject of investigation (*15*). In total, there were 16 discussion groups, four (4) from each ward. The discussion groups were stratified on the basis of age and gender.

In each ward, there were two groups of women and two groups of men differentiated by age and gender. Thus, there was one group of women 15-34 years of age and another group of men within the same age range. In addition, there was a group of women 35 years of age or older and a group of men with a similar age range. This type of stratification was done so as to give participants more freedom and flexibility to speak out about their life experiences. Each discussion group consisted of between 6-12 members and met for a period of between 1 and 1.5 h.

2.6. *Data management, processing, and analysis*

Qualitative data analysis was based on field experience. Familiarization of data was done by listening to the audio-taped information and reading through the notes and the transcripts. Codes were developed and both pre-determined and emerging themes were identified for thematic content analysis. Quantitative data, in contrast, was entered in the EPi-Info data set. Checks were made for consistency and amplitude errors and the data were transferred to STATA version 9.2 for descriptive analysis.

2.7. *Ethical considerations*

All important ethical concerns were resolved prior to data collection. The research protocol was first submitted to the national ethics review body, under the auspices of the National Institute for Medical Research, for approval and issuance of research ethics clearance. Both verbal and written informed consent were obtained from the study participants before actual data collection.

3. Results

3.1. *Descriptive quantitative findings*

3.1.1. *Introduction*

This study sought to critically assess a household's experiences with malaria and the importance of financial access networks to bear illness-related costs among people employed in informal economic activities. It also sought to identify household coping strategies and community networks to bear the costs of unpredictable malaria outbreaks. This is in line with the fact that they are not formally recognized by most health insurance schemes and other formal financial institutions due to insecurity inherent in the nature of their employment and the instability of their incomes.

3.1.2. *Socioeconomic and demographic characteristics of the study participants*

The study involved 368 participants drawn from four wards of Ilala district in the Dar es Salaam region. It was initially intended to have equal representation of men and women. At the end of the study however, men accounted for 49.45% (n = 182) while women accounted for 50.55% (n = 182). The mean monthly income for the study population was TShs 45,877 and there was no significant difference between rural and urban households. The mean age for rural households was 35.62 years while that for urban heads of households was 39.9 years.

On average, men represented a relatively higher proportion of participants who reported having a secondary education or higher. For example, out of 368 respondents only 7 reported having an education higher than the secondary level, and they were all men.

Analysis indicated that about 17% (n = 61) of the interviewees in rural and urban households reported having no formal education while 72.3% had received an education at the primary level. Overall, there were statistically significant differences ($P < 0.05$) between men and women in both rural and urban households in terms of educational level. Table 1 provides a summary of education levels of the study subjects.

3.1.3. *Forms of informal sector employment among the interviewed participants*

During analysis, two of the categories of informal sector employment (resident and transient) were omitted because all interviewees performed activities in the areas where they resided. Thus, two categories remained as shown in Table 2. The results are stratified by gender and area of residence. Of further note is the fact that while the total sample of the study consisted of 368 interviewees, analysis involved only 364 respondents (98.91%) since information on this question from four households was either ambiguous or missing, so it was omitted outright.

A Pearson Chi-Squared test indicated overall significant differences (taking the total sample into account) between men and women in terms of the forms of employment both in rural and urban households. A stratified gender analysis of both rural and urban areas indicated highly significant differences ($P < 0.001$) in terms of forms of employments. In urban households, for example, 70.16% (n = 72) of all respondents who reported being self-employed were men as compared

Table 1. Levels of education by gender and residence

RURAL			
Level of education	**Men**	**Women**	**Total**
No formal education	21.57% (*n* = 11)	22.73% (*n* = 30)	22.4% (*n* = 41)
Primary education	64.71% (*n* = 33)	74.24% (*n* = 98)	71.58% (*n* = 131)
Secondary education	9.8% (*n* = 5)	3.03% (*n* = 4)	4.92% (*n* = 9)
Tertiary education	3.92% (*n* = 2)	0.00% (*n* = 0)	1.09% (*n* = 2)
TOTAL	100% (*n* = 51)	100% (*n* = 132)	100% (*n* = 183)
	***P* < 0.028**		
URBAN			
Level of education	**Men**	**Women**	**Total**
No formal education	12.98% (*n* = 17)	5.56% (*n* = 3)	10.81% (*n* = 20)
Primary education	67.18% (*n* = 88)	87.04% (*n* = 47)	72.97% (*n* = 135)
Secondary education	16.03% (*n* = 21)	7.41% (*n* = 4)	13.52% (*n* = 25)
Tertiary education	3.82% (*n* = 5)	0.00% (*n* = 0)	2.7% (*n* = 5)
TOTAL	100% (*n* = 131)	100% (*n* = 54)	100% (*n* = 185)
	***P* < 0.042**		

Table 2. Informal sector employment by area of residence and gender

Type of employment	**Rural**	**Urban**	**Total**
Self-employed	78.33% (*n* = 141)	55.43% (*n* = 102)	66.76% (*n* = 243)
Wage earner	21.67% (*n* = 39)	44.57% (*n* = 82)	33.24% (*n* = 121)
TOTAL	100% (*n* = 180)	100% (*n* = 184)	100% (*n* = 364)
Type of employment	**Men**	**Women**	**Total**
Self-employed	68.13% (*n* = 124)	65.38% (*n* = 119)	66.76% (*n* = 243)
Wage earner	31.87% (*n* = 58)	34.62% (*n* = 63)	33.24% (*n* = 121)
TOTAL	100% (*n* = 182)	100% (*n* = 182)	100% (*n* = 364)

to only 29.41% (*n* = 30) who were women. In rural households, in contrast, women constituted a higher proportion (87.39%, *n* = 123) of those who reported being self-employed compared to 12.61% of men (*n* = 18) (*P* < 0.001).

3.1.4. *Percent of those who had malaria in the previous 14 days*

Much as the study sought to understand the extent to which lack of financial security as a result of not being employed in the formal sector can affect access to health services, understanding the level of knowledge of malaria among study participants was critical. Accordingly, lack of formal employment, which limits access to formal recognition by organized health insurance firms, was hypothesized to be one way of limiting the poor's access to essential health services.

As measured by important signs and symptoms, knowledge of malaria was greater (93%) and did not differ significantly between rural and urban households. Furthermore, about 21% of study participants experienced a malaria outbreak in their household. Table 3 summarizes the findings for rural and urban areas and for both genders.

As is apparent from the table, only 20.65% of all 368 participants (*n* = 76) reported an outbreak of malaria in their households 14 days prior to the date of the interview. The study confirms significant differences (*P* < 0.05) between men (35.53%) and women (64.47%) and between rural and urban areas, with rural households reporting more cases of the disease (75%) than urban ones (25%).

Table 3. Those who had malaria in the previous 14 days

Gender	**Rural**	**Urban**	**TOTAL**
Men	26.32% (*n* = 15)	63.16% (*n* = 12)	35.53% (*n* = 27)
Women	73.63% (*n* = 42)	36.84% (*n* = 7)	64.47% (*n* = 49)
TOTAL	100% (*n* = 57)	100% (*n* = 19)	100% (*n* = 76)
	***P* < 0.004**		

When the data were divided into rural and urban areas, women in rural households bore a greater burden of malaria than men. The picture in urban households differed since men experienced more outbreaks of malaria than women. This finding, though seemingly complex, can partly be explained by the fact that in most traditional African households in rural areas women shoulder a double (if not triple) work load of caring for children and caring for the entire family (despite their special reproductive health care needs). This phenomenon may partly increase women's exposure to mosquito bites within and without their homes in their efforts to ensure that households are

provided with both needed health care and other resources to survive.

In urban areas, in contrast, higher prevalence among men may be due to their exposure to outside chores that are related to both working long hours for a living (and sometimes at night, as much domestic work is done by women) and their almost unrestricted movements outside their homes at night to participate in different leisure activities.

3.1.5. *Number of malaria outbreaks by gender and area of residence*

Frequency or recurring patterns of illness (in this case, malaria) have direct implications on costs. Without adequate mechanisms of financial risk protection, the effects of illness especially among low income earners may be fatal. Table 4 summarizes and compares reported outbreaks of malaria between the two genders.

3.1.6. *Hospitalization by gender and area of residence*

Out of the 21% (n = 76) of interviewees who reported an outbreak of malaria in the previous two weeks, only 15.8% of cases (n = 12) required hospitalization. Though the difference was not statistically significant, there was a higher rate of hospitalization in rural households (17.54%, n = 10) than in urban households (10.53%, n = 2). The rate of hospitalization among women was 16.33% (n = 8) while among men it was 14.81% (n = 4).

Stratified analysis by area of residence revealed a statistically significant difference ($P < 0.05$) between men and women in terms of hospitalization rates. Out of a total of 19 cases of malaria in urban households, all of those that required hospitalization (28.57%, n = 2) were women.

In rural households (where 59 interviewees reported an outbreak of malaria in their households), out of 15 reported cases the rate of hospitalization among men was 26.67% (n = 4) while it was 14.29% among women (n = 6). Gender differences within rural households were, however, not statistically significant.

3.1.7. *Health-seeking behavior*

Health-seeking behavior was of considerable interest in this study because evidence is limited concerning access to and utilization of health services among informal sector employees in developing countries. A majority of people working in the informal sector largely depend on government/public health services, with women reporting more use of health care than men (Table 5). This 'public-facilities-dependence-pattern' did not differ between rural and urban areas or between women and men.

Health-seeking behavior may be affected by a multitude of factors ranging from a household's socioeconomic characteristics, perceived quality of health care services, and other 'access' barriers such as distance to a health facility. This study revealed that rural households are on average located further away

Table 4. Reported outbreaks of malaria in the previous fourteen days prior to the interview

A: No. of outbreaks	Men	Women	Total
1	37.04% (n = 10)	57.14% (n = 28)	50% (n = 38)
2	51.85% (n = 14)	38.78% (n = 19)	43.42% (n = 33)
3	7.41% (n = 2)	4.08% (n = 2)	5.26% (n = 4)
4	3.70% (n = 1)	0.00% (n = 0)	1.32% (n = 1)
TOTAL	100% (n = 27)	100% (n = 49)	100% (n = 76)
B: No. of outbreaks	**Rural**	**Urban**	**Total**
1	45.62% (n = 26)	63.16% (n = 12)	50% (n = 38)
2	47.37% (n = 27)	31.58% (n = 6)	43.42% (n = 33)
3	5.26% (n = 3)	5.26% (n = 1)	5.26% (n = 4)
4	1.75% (n = 1)	0.00% (n = 0)	1.32% (n = 1)
TOTAL	100% (n = 57)	100% (n = 19)	100% (n = 76)

Table 5. Proportion of men and women and the source of health care from which they sought care for a malaria outbreak in the previous two weeks

Source of care	Men	Women	TOTAL
Government pharmacy	74.08% (n = 18)	73.58% (n = 37)	72.37% (n = 55)
Government health center	3.70% (n = 1)	3.77% (n = 2)	3.95% (n = 3)
Government hospital	3.70% (n = 1)	5.66% (n = 3)	5.26% (n = 4)
Private health center	3.70% (n = 1)	0% (n = 0)	1.32% (n = 1)
Private hospital	7.41% (n = 4)	16.98% (n = 6)	14.47% (n = 10)
Traditional healer	7.41% (n = 2)	0% (n = 1)	2.63% (n = 3)
TOTAL	100% (n = 27)	100% (n = 49)	100% (n = 76)

from health facilities (health centers and hospitals) than their urban counterparts. Arguably, this may represent a barrier to seeking health care especially when costs of transport and opportunity costs of time (as a result of walking long distances) are taken into account. Table 6 presents the results by comparing rural and urban households' proximity to a nearby health center/ hospital.

3.1.8. *Coping strategies for malaria-associated costs*

As has been generally indicated in preceding sections, most of the heads of household interviewed had either limited access to formal financial institutions or had very limited cash profits as would allow bank savings.

Moreover, among those who reported an outbreak of malaria in their households, none reported being a beneficiary of any form of health care insurance. Though bank savings is not the only feasible option to survive a catastrophic event resulting from malaria, evidence is surfacing to indicate that such savings are a potentially viable and effective tool among people who are not considered 'insurable' by health insurance companies (both private and public) or who are not considered creditworthy by other lending (financial) institutions. In this study, participants identified a number of options that were adapted and adopted accordingly when financial costs related to malaria were considerable (Table 7).

3.1.9. *Access to and membership in formal financial institutions*

Out of 368 participants, only 27.99% (n = 103) had an active bank account at a formal financial institution (such as a Micro-finance institution). Not surprisingly, though, interviewees from urban households reported a significantly higher proportion ($P < 0.01$) of members with an active savings account at a formal financial institution at the time of the interview.

Of all 103 interviewees who reported having a bank account, those from urban households accounted for 64.08% (n = 66) while those from rural households accounted for 35.92% (n = 37). This may be explained by the tendency of many of these organizations to be concentrated in urban areas rather than in rural areas. The findings further highlight significant gender differences both among rural and urban households. In rural households, for example, about 63.64% of women (n = 21) had an active bank account compared to 22.86% of men (n = 16) ($P < 0.05$).

In urban households, the picture is reversed in that a significantly higher proportion of men (77.14%, n = 54) had a bank account compared to women (36.36%, n = 12) ($P < 0.05$). Among those who reported an outbreak of malaria (20.65%, n = 76) in the 14 days prior to the date of the interview, only 13.16% of interviewed heads of household (n = 10) said that they had an active bank account.

Though the significance of the differences between rural and urban areas and between both genders could not be tested due to limitations imposed by the size of the sub-sample (n = 10), calculated proportions indicated that among those who reported an outbreak of malaria in their households, women (80%, n = 8) had a higher participation in networks with formal financial institutions. Unexpectedly, most were from rural households where bank facilities are somewhat wanting.

3.1.10. *Membership in informal savings groups*

Informal networks to secure financial services were highlighted as an important coping strategy for people employed in the informal sector especially when they were hit by an outbreak of malaria in their households. Figure 1 highlights some of the findings and compares households' participation by area of residence.

In total, more than 80% of the study participants

Table 6. Distance to a nearby health center/hospital

Distance	Rural	Urban	TOTAL
Within 5 km	45.61% (n = 26)	84.21% (n = 16)	55.26% (n = 42)
10 km	50.88% (n = 29)	15.79% (n = 3)	42.11% (n = 32)
More than 10 km	3.5% (n = 2)	0.00% (n = 0)	2.63% (n = 2)
TOTAL	100% (n = 57)	100% (n = 19)	100% (n = 76)

Table 7. Coping strategies to bear malaria-related costs

Coping strategy	Rural		Urban		TOTAL
	men	women	men	women	
Borrowed money from informal credit association	13.33% (n = 2)	35.71% (n = 15)	41.67% (n = 5)	42.86% (n = 3)	32.89% (n = 25)
Sought assistance from employer	0.00% (n = 0)	4.76% (n = 2)	8.33% (n = 1)	0.00% (n = 0)	3.95% (n = 3)
Sought assitance from relatives	60% (n = 9)	42.86% (n = 18)	16.67% (n = 2)	42.86% (n = 3)	42.11% (n = 32)
Borrowed from friends/neighbors	26.67% (n = 4)	16.86% (n = 7)	33.33% (n = 4)	14.28% (n = 1)	21.05% (n = 16)
TOTAL	100% (n = 15)	100% (n = 42)	100% (n = 12)	100% (n = 7)	100% (n = 76)

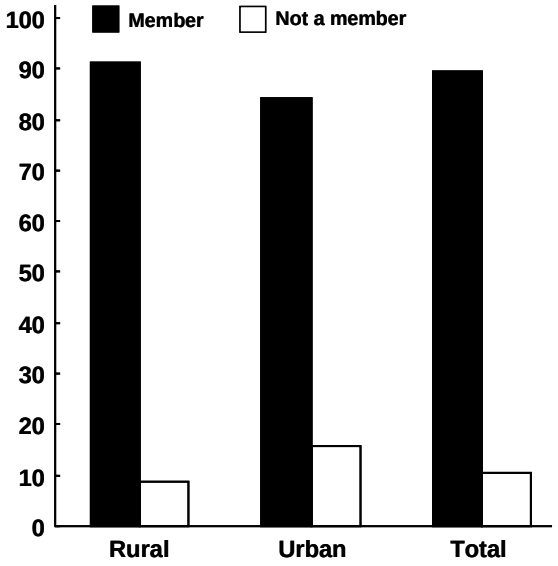

Figure 1. Membership in informal savings and credit organizations.

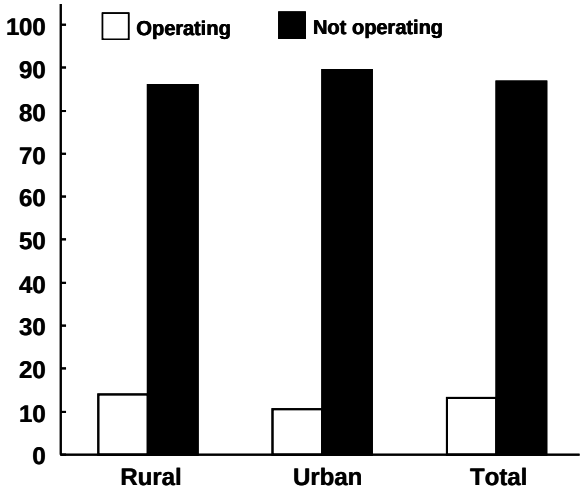

Figure 2. Proportion of rural and urban residents with an active savings account at a formal financial institution.

participated in some kind(s) of informal financial arrangements. Though evidence on the feasibility and sustainability of these arrangements is limited, this finding indicates that relevant authorities should consider the formally unemployed to be creditworthy and amenable to mainstreaming into formal structures of financial credit systems. This is crucial because the current state of affairs is such that people who are in the informal employment sector have extremely limited participation in formal financial banking systems where loans/credit can be obtained.

Though further research remains, the observed pattern may partly be explained by their (employees in the informal sector) limited willingness, or total lack thereof, to participate in and/or inability to afford banking services. Traditionally, most formal financial institutions prefer to deal with the formally employed rather than the unemployed.

The economic rationale for this tendency is related to the need to reduce transaction costs and uncertainty about the creditworthiness of the poor and informally employed. Figure 2 highlights the proportion of study participants with a savings account at a formal financial institution.

3.2. *Findings based on qualitative data*

3.2.1. *Perception of malaria as a health risk requiring adequate mechanisms of financial protection*

The majority of participants confirmed that the disease (malaria) negatively impacted the day-to-day social and economic activities of the household's members.

"On all fronts, malaria has had a devastating effect on our lives both at the household and community levels. When one member of the household is hit by recurring outbreaks of malaria, this implies that other productive economic activities have to be foregone and sometimes even limited financial resources have to be diverted towards bearing the costs of treating the ill person." (urban female FGD participant)

Although malaria is perceived as catastrophic both socially and economically, discussion sessions have consistently confirmed a higher level of awareness of the direct and indirect effects of redefining households' decisions in allocating financial resources. In some extreme scenarios, money that was initially set aside to pay for, say, children's school fees had to be re-allocated (diverted) to bear the costs of treatment.

"Most of us are actually poor, but there are some of us who are even poorer. It takes one or two outbreaks of malaria for these households to completely fail to bear some costs of education such as buying textbooks. Thank the government that primary education is provided freely, but children need not go to school hungry. In most poor households, they can afford only one meal a day but it is of poor quality and sometimes not enough meet actual nutritional requirements per person per day. In essence, the point is not about diverting financial resources to bear the cost of treatment but that there is sometimes no other way but to prioritize." (rural male participant)

3.2.2. *Hardship in relation to households' efforts to seek medical treatment*

While frequent malaria outbreaks have consistently been cited as one way poor households are drawn deeper into a medical poverty trap, additional hardships, and especially those related to looking for medical treatment, had been mentioned. This is even

more noticeable among mothers who spend much of their time making periodic trips to pharmacies and health centers/hospitals to seek care for themselves or other family household members, and especially infants and children under five. One participant, for example, pointed out that:

"In a situation when you do not have money to take your child to a nearby private health facility or buy medicine to bring the child's fever down, you are forced to walk long distances to health centers and sometimes you just leave home without even eating breakfast. After arriving at the facility, you then wait too long for someone to see you. Upon returning home, you are hungry and exhausted but you have to deal with other domestic chores such as collecting firewood, fetching water, and cooking for the rest of the household. Sometimes you do not have enough sleep because you have to monitor the child's temperature as a result of a malarial fever. All this means that your health weakens day after day." (urban female participant)

The agony due to death of a loved one as a result of malaria has also been consistently noted as a hardship.

"Several times, deaths have caused psychological hardships for families who are already struggling with the heavy burdens of poverty. The hardship is even worse when the death involves the household's primary breadwinner." (urban female participant)

Inability to hire private transport or the potential unavailability of such services especially in rural areas has resulted in a number of child deaths on the way to health facilities.

"You know, when a child has 'degedege' (literally meaning convulsions), there are still a few people who believe that a child must be 'prepared' by a traditional healer or just given a traditional medicine before being taken to the hospital. In most cases, this delays the process of receiving appropriate medical care and complicates the illness, sometimes leading to death. We have seen and read in the papers of children dying after just arriving at the health facility or dying on the way to the hospital especially when receiving available care means walking a long distance." (urban male participant)

3.2.3. *Willingness to borrow money from formal financial institutions to bear the costs of illness*

FGD sessions indicated that a majority of participants noted the importance of being networked with formal financial institutions both to help them strengthen their capital base as well as to allow them to use financial resources to respond to a catastrophic event resulting from an outbreak of malaria. A major limitation that was consistently identified as hindering access to formal financial institutions was the inability to meet the eligibility criteria that most lending institutions require to be considered creditworthy.

"Some of us have tried several times to ask the bank people about the possibility of taking out small loans from their banks. But the criteria that they always give mean that a bank is not the right place to go if you do not have stamped papers from an employer in the formal sector or if you do not possess assets such as a house or a car. And you know most of us have no chance of owning these." (rural female participant in an FGD)

"If they decided to give us a loan, we would never use the money for one-off events like a funeral or wedding. Instead, they must know that we are able to invest the money in economic activities; after making a profit, money can be allotted to normal expenditures including bearing the costs of illnesses such as malaria." (urban female participant in an urban FGD session)

While loans can essentially be used to enhance or improve economic enterprises, they can also be used as a 'malaria shock absorber', *i.e.* the impact on both the health of the members of the affected household as well as on the household's potential economic ability to disentangle it from the medical poverty trap.

3.2.4. *Borrowing from friends and neighbors as a coping strategy*

Most households that fail to bear the costs of malaria treatment, and especially when an outbreak requires hospitalization, find themselves in great debt as they try to bear the costs of daily living and other financial burdens as a result of a member of the household falling ill. Indebtedness, poverty, and illness further complicate their lives as they struggle to deal with the triple burden of disease, poverty, and the obligations to repay the loan/debt. One participant, for example, observed that:

"Due to persistent indebtedness as a result of our children's illness, we frequently find ourselves unable to meet even the family's most basic nutritional needs… when a child is so poorly fed, even a slight fever can take his or her life." (rural female participant)

3.2.5. *Selling labor as a coping strategy*

Selling labor begins as a result of three causes. First is the need to supplement household income to meet daily needs, second is the unpredictable nature of the need to bear illness-related costs as a result of malaria, and third is the repayment obligations created by indebtedness. As cited by one participant,

"To meet loan/credit repayment obligations, one has to pay dearly in kind. This may mean either working on the lender's farm or giving him produce equivalent to the money borrowed. In most cases, however, the payment is worth more than the original amount of money borrowed." (rural male participant)

3.2.6. *Building 'trust' networks with shop owners and health workers at private health facilities and pharmacies as a coping strategy to bear malaria-related costs*

Discussion sessions revealed that despite the growing trend of self-medication, some households have established stable credit patterns that allow them to obtain malaria drugs from nearby pharmacies under the condition that they will pay immediately once they have the money. This is especially true in urban areas, where there are relatively well-established networks of shops and private pharmacies/drug stores. Obviously, however, such lending depends on one's residency, *i.e.* such lending is only possible when one is known to have resided in the area for a reasonable number of years (normally about 5+ years).

The economic rationale for working with private facilities and pharmacies originates because of the unpredictability of malaria outbreaks, especially among children under five. One participant commented that:

"We know that children under five years of age are supposed to receive free treatment at government health facilities, but sometimes a child unexpectedly falls ill and you need to hire a private taxi to quickly reach a nearby health facility. The cost may be more than Tshs. 4,000/=, and there is no guarantee that you will have the money at that time… So if you are known and trusted by one or two of the private health facilities, you can quickly take the child to receive treatment and stop at a nearby shop/pharmacy to obtain drugs prescribed by the doctor but that are not available at the hospital." (urban female participant)

3.2.7. *Informal credit networks as a source of money for malaria treatment*

Informal networks of both men and women have consistently been mentioned as a source of money to bear malaria-related costs.

"We are involved in what is widely known as 'Upatu'- (a Swahili word, literally meaning a form of savings and credit arrangement in which a group of people contribute a specified amount of money to their fellow member(s) on a rotating basis, one member after another)."

"...When your turn comes, life is a little more relaxed... well, it may be little money, but because you already have a small business going, you have the time to expand the capital base of your business, especially when no one in the family is sick. The money may also be used to cover any illness-related costs if, unfortunately, someone falls ills at the same time when the money is due." (urban female participant)

Criteria for membership eligibility in this form of savings-and borrowing ('*Upatu*') is framed so that accountability is based on the principles of trust and reciprocity, as there are no formal contractual agreements among the members. Furthermore, use of *upatu* was consistently more common among women than men. Not apparent, however, is whether or not men are more averse than women to the core principles ('trust' and 'reciprocity') defining *Upatu*-membership. Longitudinal studies are needed to quantify the patterns observed.

3.2.8. *Awareness of the existence of established forms of Health insurance (e.g. Community Health Insurance Fund)*

Though the study did not initially intend to inquire about the existence of Community health insurance around the country, discussions did reveal that study participants were aware of the existence of community health insurance in the country but were not sure whether it did operate in Dar es Salaam region but not sure if it operated in the Dar es Salaam region. While the scheme was not available at the time of this study, many participants emphasized the need to be integrated if the scheme operated in the region or to be provided with appropriate information on other established forms of health insurance. This confirms the willingness of informal sector employees to pay for community health insurance.

3.2.9. *Recommendations to help informal sector employees reduce their barriers to seeking modern health care services*

Though examination of what works and what does not is crucial, FGD participants proposed a number of recommendations as a way to ensure the financial security to be able to bear the costs of health care access and utilization in the event of a malaria outbreak. The following is a summary of points cited consistently in discussion sessions. Education and information about health insurance should be provided, and organizations providing these services need to be 'community grown'.

Formal financial institutions such as health insurance companies (both private and public) and banks need to introduce flexibility in the ways in which informal sector workers can obtain health insurance membership. Similar flexibility is needed when

borrowing money from banks to help cope with both the costs of ill health and other basic needs.

The often-heard pronouncement that the country's (Tanzania) economy is growing at a relatively good pace should translate into more jobs to enable people in informal sector employment to be formally employed and consequently covered by available health insurance schemes.

Finally, tax contributions from the formally employed and other sources should be earmarked to subsidize health care costs for the poor in informal sector employment and the unemployed. The earmarked taxes should form a type of insurance fund that is targeted to specific, common illnesses afflicting the poor (anemic malaria for children under five and pregnant mothers, cerebral malaria, *etc*.) since they often need hospitalization.

4. Discussion

The current analysis was driven by the recognition of the importance of informal sector employees in the context of a developing country like Tanzania in relation to their need in gain access to modern health care services.

Like in many developing countries, the informal sector in Tanzania is growing at a rapid pace, and its contribution to the overall economic situation cannot be underestimated. Their lack of recognition in the formal credit systems and formal health insurance arrangements and formal health insurance arrangements make them more vulnerable to financial risks of illness especially in a country where diseases such as malaria are so prevalent.

This study has provided critical insights regarding informal sector employment and practicalities in bearing the financial costs of gaining access to essential medical care in times of malaria outbreaks. Although there are different coping strategies among informal sector employees, informal savings networks are significant in not only helping households to cope with financial shocks caused by malaria but also in overall attempts by the poor (informally employed and unemployed) to disentangle themselves from the medical poverty trap.

A further finding has been that informal sector employees are willing to both be covered by existing forms of health insurance and also be integrated into the formal banking system. The policy implications of this finding point to the need to review existing eligibility criteria that bar the poor and particularly informal sector employees from gaining access to credit services provided by banks and from being covered by formal health insurance arrangements.

Even when there was a greater willingness to both be integrated into formal banking systems and to be covered by formal insurance arrangements, there was an apparent uneven distribution of these facilities between rural and urban areas. This is, however, not surprising because of the economic rationale inherent in the operations of banking and health insurance businesses. That is, demand factors will always determine where services are located/provided. In other words, urban more than rural areas are considered to be attractive to investors because of the presumed greater willingness and ability to pay of a higher proportion of the inhabitants.

Analysis also revealed that malaria is considered to be both a health and an economic risk. The coping strategies that were identified indicated that catastrophic shocks caused by illness are directly associated with economic vulnerability, which translates into households' inability to actively engage in productive economic activities and their failure to respond to financial shocks caused by illnesses. This finding is consistent with the concept by Whitehead *et al.* (*2*) of the 'medical poverty trap'.

Although there were significant differences ($P < 0.05$) between rural and urban households and between men and women in terms of forms of employment, educational achievements, prevalence of malaria, and hospitalization rates, mechanisms of coping with malaria-related costs of treatment were not, however, statistically significant. This explains why literature on the disposition of informal sector employees is in relative agreement and the employees thus respond to the financial crises caused by illness in more or less similar ways.

Rural households on average appear to travel longer distances to health facilities than their urban counterparts. This implies that while both rural and urban households face more or less the same level of vulnerability to outbreaks of malaria, rural residents are faced with yet another burden of walking longer distances to health facilities along with negative consequences of increased costs of transport.

There is also another issue of the possible higher opportunity costs due to time spent walking to facilities and possibly waiting too long before being attended by health workers. This again highlights the need for targeted efforts towards equitable distribution of health facilities and other medical resources in accordance with need.

The finding that a statistically significant ($P < 0.05$) proportion of women in rural areas came under the category of those who are 'self-employed' suggests increased decision-making ability among rural women. In terms of policy implications, targeted efforts are needed to unleash the full potential of women as active players in economic production as well as to encourage appropriate decision-making regarding their health and that of other members of the households.

The cross-sectional nature of the current study prevented the determination of any causal relationships

between the variables employed in the study. Potential research hypotheses, however, can be formulated for testing in the Tanzanian health insurance market, which is still in its infancy. In addition, the mean monthly incomes of the households may be grossly underestimated. This may be because of the fact that most people, and especially those in developing countries, are reluctant to reveal their real income and there are no reliable mechanisms (like an efficient and reliable tax information system) by which peoples' real income can be tracked. Although not used in the current study, the best way to obtain a 'proxy' for this information would be to collect data on household assets and compute a wealth index.

While there are already government efforts to subsidize the majority of people (the poor in formal and informal systems and the unemployed) through tax-based expenditures on health care, tax-based financing of health care is not only inadequate but may also be poorly or ineffectively targeted. It may thus end up benefiting those in the formal sector who are able to pay for their health care costs through different 'open' and 'employer-based' health insurance mechanisms. Such distorted cross-subsidization is regressive and therefore inequitable.

Since not all people in the informal sector are essentially poor, critical willingness and ability-to-pay studies (ability to pay for formal health insurance) must be conducted among the people who are in informal sector employment. In this event, a research hypothesis could be that people employed in the informal sector have different levels of willingness and ability to pay for health insurance services.

Even though there were signs of willingness to pay for formal health insurance (levels of willingness and ability to pay for the poor and non-poor is not known), any policy decision to incorporate informal sector employees should be carefully designed to take into account factors such as administrative costs due to difficulties in monitoring membership, adverse selection among potential members, and perverse incentives inherent in health care systems that may discourage enrollment of those who have already shown a willingness to participate.

5. Conclusions

The qualitative findings, descriptive figures, and statistics as shown thus far suggest some basic facts, some a little bit surprising, but most are fairly consistent with the established body of evidence. They do, nonetheless, lead to two conclusions.

First the consistent nature of the current findings with those of Whitehead *et al.* (*2*), in that some coping strategies such as borrowing from friends and neighbors have a greater tendency to drag households further into medical poverty, suggests that there is a need for health systems to respond by supporting communities' efforts to establish sustainable financial networks. Similarly, these systems must work towards removing perverse incentives that may prevent those working in the informal sector from taking advantage of available health insurance arrangements. Existing protection and health insurance mechanisms available in Tanzania must be reconfigured.

Second, as observed by the World Health Organization (*16*) when referring to distribution of health facilities in most Sub-Saharan African countries, the current study found that rural households were on average further away from health facilities than their urban counterparts. The policy implications of this finding are that health facilities in Tanzania are either unevenly distributed between rural and urban areas or that those facilities close to consumers are perceived as being unable to provide the quality of care expected by users and potential users. To this end, efforts are necessary to ensure that health facilities are provided with the resources (human resources, drugs, equipment, *etc.*) needed to effectively provide quality care and they must be nearby as prescribed by national and international health policy standards. While attempting to achieve this goal amidst competing priorities and limited health care resources may sound idealistic, 'earmarking' some tax resources and 'targeting' the rural poor represents an optimal short-term solution.

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Original Article

Training health professionals to detect and support mothers at risk of postpartum depression or infant abuse in the community: A cross-sectional and a before and after study

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Summary **The purpose of this study was to evaluate the 2-day seminar in 2 consecutive years respectively for community health professionals. We prepared the child-rearing support manual (CRSM) and conducted a seminar program to improve skills to provide mental assessments and postnatal care support for mothers and their families in the community using the CRSM. After the seminar in the first year, the first questionnaire was performed regarding the participants' expertise, skills, and system of operations of their facilities. After the seminar in the second year, the same questionnaire was administered. In addition, a questionnaire survey was also administered on the use of the CRSM, *etc*. for all prefectural health and welfare centers around the nation. As a result, it was found that the participants in both seminars showed significantly higher scores regarding expertise and skills compared with the other participants who had not participated in the seminar in the first year. In comparison of the participants in both seminars between their responses of the first and the second year, significant increases were confirmed in the score of interpersonal health care skills and in the score for system of operation at their institutions. In addition, it was found that the CRSM was used in approximately half of the institutions around the nation. The authors concluded that this seminar program was effective in developing the expertise and skills of individual health professionals, the system of operation of their institutions, and community maternal and child mental health in the nation.**

Keywords: Child abuse, Depression, Postpartum, Program evaluation, Public health professional

1. Introduction

Postpartum depression is one of the depressive disorders observed in women after childbirth, and can develop at a high rate within one year after childbirth; 10-15% in several countries (*1,2*). Although the most frequent period of development has been described as 4-6 weeks after childbirth, it has been recently clarified that the disease most often occurs even earlier; a couple of weeks after childbirth (*3,4*). As well as having a negative impact on the child-rearing function of the family and the development of infants (*5*), postpartum depression is considered to be one of the risk factors for infant abuse (*6*). The Japanese Ministry of Health, Labour and Welfare has designated the decrease in the incidence of postpartum depression and mortality due to child abuse as the major objective of the project named "*Sukoyaka Oyako* 21 (*Sukoyaka* Family 21: *Sukoyaka* means sound or well-being)". There is an urgent need to establish preventive measurements for inappropriate childcare or infant abuse, including early screening of

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postpartum depression.

Dennis undertook a systematic review to assess the effects of psychosocial and psychological interventions compared with usual antepartum, intrapartum, or postpartum care on the risk for postpartum depression (*7*). She concluded that diverse psychosocial or psychological interventions do not significantly reduce the number of women who develop postpartum depression, but she described that home visits by a health professional were clearly proven to be effective in two trials (*8,9*). Since the Imperial Gift Foundation Boshi-Aiiku-Kai (Mother-Child Nursing Association) was founded in 1934, the Japanese maternal and child health system, including newborn visits, has been supported in communities by volunteer laypersons, such as a Mother-Child Nursing Team. Recently, the program of newborn visits by health professionals, mainly from health and welfare centers in the community, may have contributed towards decreasing the anxiety of mothers regarding child rearing (*10*). The Japanese Ministry of Health, Labour and Welfare designated the new project named "*Kon'nichiwa Akacyan* (Hello-Baby)", in which health professionals should visit all of the newborn babies and their mothers within four months after birth. We considered that improvement of the skills of health professionals, who visit mothers to support their postpartum mental health, would be a practical and effective way for early screening of postpartum depression and to implement preventive measures for infant abuse.

The Edinburgh Postnatal Depression Scale (EPDS) is a self-administered questionnaire developed by Cox *et al*. for population-based screening of postpartum depression (*11*). It has been shown that use of this questionnaire can increase the population-based detection rate of postpartum depression. Okano *et al*. developed the Japanese version of the EPDS, and identified that the cutoff point of a clinical concern for postpartum depression was 8/9 (*12*).

After using the Japanese version of the EPDS (*12*) at newborn visits in Fukuoka since 1998 (*13*), Suzumiya and Yoshida expanded its use to 38 health and welfare centers in communities in 2002, and identified that 10.5-13.9% of newborn mothers exhibited postpartum depression (*2*). Moreover they confirmed the usefulness of the method in which health professionals who perform postnatal visits utilized the EPDS (*11,12*) and the Mother's Attachment to Baby Scale (MABS) (*Marks, unpublished*; *13*); in combination with a check list of risk factors regarding postpartum depression and infant abuse, which includes socioeconomical items (*2,13*). In 2004, the Child-Rearing support manual (CRSM) was developed, based on these three types of questionnaires, using the Grants for Health Science (Research on Children and Families) (*14*), and was freely distributed to 127 main branches of maternal and child health organizations in Japan (in 47 prefectures, 13 government-designated cities, 9 public health center-designated cities and 23 wards of Tokyo). In addition, using this CRSM, a training seminar was scheduled in 2005 and 2006 for health professionals who make postnatal visits. The purpose of this seminar was to improve the skills of health professionals who provide mental assessments and postnatal care support for mothers and their families in the community, and to improve the establishment of measures for the mental health of mothers and children.

The objective of this study was to evaluate the results of the seminar performed for community health professionals over 2 years from the following 2 perspectives.

1) The level of personal expertise and support skills of community health professionals, and the operational level of support activity for the postnatal mental health of mothers at institutions for in each health professional worked.

2) The level of expansion of support activity using the CRSM for the postnatal mental health of mothers around the nation.

2. Methods

2.1. *Training Seminar*

The 2-day seminar titled "Seminar for the postnatal mental health of mothers and child rearing support" was held in Tokyo and Fukuoka in August and September in 2005 and 2006, respectively. As the materials for the seminar, the CRSM and paper patient were used. As teaching methods, lecture, group work and presentation by participants were utilized.

The seminar held in 2005 included 1) "Basic knowledge for the postnatal mental health of mothers (postpartum depression, bonding disorder, *etc*.)" (90 min), 2) "Details and methods of support (details and use of 3 types of self-administered questionnaire sheet)" (90 min), 3) "How to describe cases" (60 min), 4) "Assessment at home visits and how to perform careful interviews" (120 min), and 5) "Planning of support, continuous support, and evaluation" (180 min).

Based on the results of the first self-administered questionnaires in December 2005, it was found that there was significant need for lectures on the concrete use of the EPDS and supervision for support of the cases with specific backgrounds (*15*), and that it would be important to make an image of successful support for various cases (*16*). Furthermore, one month before the seminar in 2006, a structural description of the cases for which continuous support was completed was requested of the 209 persons who were scheduled to participate in the seminar, through the web site of a collaborative researcher to determine the details of the seminar to be held in 2006.

As a result, the details of the seminar in 2006 were determined as follows. In 1) – 5), lectures were

held, and in 6), after obtaining an agreement from the participants, simulated supervision of cases selected from those submitted by participants was performed by several supervisors. 1) "The use of 3 types of questionnaires and several examples of activity in local communities" (100 min), 2) "Organizational cooperation: from support in local communities to the introduction of psychiatric clinics" (80 min), 3) "The use of 3 types of questionnaires and countermeasures for infant abuse – Based on the high-risk cases of infant abuse –" (80 min), 4) "From anxiety for child rearing to infant abuse – for mothers with problems bonding to their children –" (60 min), 5) "Educational seminar methods and their effects" (30 min), 6) "Case supervision" (120 min): a) Advice for the mothers with anxiety regarding child rearing and support in local communities, b) Countermeasures for mothers with postpartum depression: continuous support in local communities or the introduction of psychiatric clinics, and c) Continuous support for the cases of infant abuse in local communities and points of cooperation with other institutions, and 7) Questions and answers (70 min).

2.2. *Study No. 1*

2.2.1. *Participants and procedures*

Firstly, we advertised the seminar through the website of the Mothers' and children's Health & Welfare Association, as well as through the mail to 127 main branches of maternal and child health organizations around the nation, to which the CRSM was distributed in 2004, to request they extend notification of the seminar to related facilities in their catchment areas. The seminar was held in Tokyo and Fukuoka, and 232 health professionals participated in the seminar held in 2005 from Tokyo, Hokkaido, and 37 prefectures. In 2006, a leaflet was sent to the 232 participants from the seminar held in 2005, and the seminar was advertised through the 127 related main branches of maternal and child health organizations and the website, as was done for the first seminar. Since the seminar in 2006 was held as follow-up for the participants in the seminar in 2005, when a participant from the seminar in 2005 was transferred to other institution, his or her colleague in the former institution was invited to participate in the seminar in 2006. For the institutions in which no one had participated in the seminar in 2005, health professionals who had the same level of basic knowledge as the participants in the seminar in 2005 were encouraged to participate in the seminar in 2006. As a result, 209 health professionals from Tokyo, Hokkaido and 34 prefectures participated in the seminar held in Tokyo and Fukuoka in 2006. They included 105 from the institutions that participated in the seminar in 2005, and 104 new participants.

It was advertised publically that the seminar would be performed as part of a research activity. An oral explanation of the objective of the research was provided on the day of the seminar. The fact that the signed questionnaires would be strictly managed and published without identifying individuals and the institutions where they worked was also explained. Subjects were sent the first self-administered questionnaires by mail in December 2005. In addition, subjects were handed the second questionnaires on the day of the seminar in 2006. Written consent to participate in the research was obtained in both 2005 and 2006.

2.2.2. *Measures*

In the questionnaire, demographic data of participants and their institutions was obtained, and original scales for expertise, skills and operation level were used for evaluation of the outcome of the seminar program. This was because reliable and appropriate scale was not available to measure expertise and skills of community health professionals that were required for home visits and other activities for maternal and child mental health support. The scales were prepared based on the scale used in the seminar held by Elliott *et al*. (*17*) for health visitors and the scale developed by Saeki *et al*. (*18,19*) to measure the practical competence of public health nurses who worked for Japanese local governments, as well as the CRSM that had been established, as described above, through activities in Fukuoka.

The scale for expertise was prepared with 15 items and 3 factors, such as Factor 1: knowledge of postpartum mental health, Factor 2: knowledge of details and how to interview postnatal mothers using the 3 types of questionnaires, and Factor 3: knowledge of how to use the 3 types of questionnaires for continuous support for mothers. The questionnaire had a 4-point Likert scale, with points ranging from 1 (not known at all) to 4 (well known). The Cronbach's α values for the total, first, second, and third factors in the participants in the seminar in 2006 were 0.95, 0.88, 0.96, and 0.95, respectively.

The scale for skills was prepared with 10 items and 2 factors, such as Factor 1: interpersonal health care skills, and Factor 2: skill at formulating measures (*16*). The questionnaire had a 4-point Likert scale, with points ranging from 1 (insufficient) to 4 (sufficient). The Cronbach's α values for the total, first, and second factors in the seminar in 2006 were 0.92, 0.92, and 0.88, respectively.

The scale for operational level was prepared to examine whether an institution had an established operation system or not, and included 6 items and 1 factor. In addition, an open question was made regarding the expectation for establishment of operation system within the next year.

2.2.3. *Design*

The participants in the second evaluation were divided into 3 groups: those who participated in both seminars held during the 2 years (Group A), those who were colleagues of participants in the first seminar from the same institution (Group B), and those who participated in the second seminar after they indicated that they had basic knowledge on postpartum mental health and home visits using the EPDS, *etc*., although they had not participated in the first seminar (Group C). In addition, those who participated in both the first and second evaluations were defined as Group A'. Firstly, the background of the A, B, and C groups was examined using ANOVA, χ^2 test, and Fisher exact-test. Then, after examining the difference between the 3 groups using ANOVA regarding the scales for expertise, skills, and operational level, we determined the 2 groups with a difference using Bonferroni's multiple comparison. Next, the difference in the average point of the individual scales in Group A' between the first and second evaluations was examined using paired *t*-test. The test was performed as a two-sided test, and significant difference was confirmed when significance probability was $p < 0.05$. For analysis, the statistical analysis package SPSS12.0J for Windows was used.

2.3. *Study No. 2*

2.3.1. *Participants and procedures*

The research was performed for all of the prefectural health and welfare centers ($n = 394$) around the nation. Since the name of the target department varied, the individual "persons in charge of maternal and child healthcare activities in the municipalities" were requested to fill in and return the questionnaires. For this research, the questionnaires were sent with the explanatory leaflet clearly describing that the results would be provided to all prefectural health and welfare centers and individual municipalities, that the answers would be processed statistically and individual health and welfare centers would not be identified, that the data obtained would not be used for objectives other than that of the study. The request was provided with a letter signed jointly by the Department of maternal and child health and the Department of general affairs Section of abuse prevention, Equal employment, children and families bureau, the Ministry of Health, Labour, and Welfare. When receiving the answers, we considered that the senders agreed to participate in the research. The study was performed from November 2007 to February 2008.

2.3.2. *Research items*

The research items related to demographic data included job title of the person who filled in the questionnaires, location of the health and welfare center and the scale of the area managed by the health and welfare center. In addition, a question was posed regarding the use of the CRSM.

2.3.3. *Design*

The descriptive statistics value was measured. For analysis, Microsoft Excel office 2007 was used.

3. Results

3.1. *Study No. 1*

Although the number of collected answers in the second evaluation was 133 (collection rate: 63.6%), the number of effective answers was 116 (effective answer rate: 55.5%) because 17 were excluded in the total, including those whose participation in the first seminar could not be confirmed ($n = 8$), those who did not fill in the column of agreement in the consent form ($n = 4$), and those who filled in less than 70% for one or more scales ($n = 3$). Groups A, B, and C included 37, 40, and 39 participants, respectively (Table 1). Regarding the demographic data of the participants, it was found that 114 (98.3%) were female, 100 (86.2%) were public health nurses, 12 (10.3%) were midwives, 2 (1.7%) were nurses, and 1 (0.9%) was a physician. Their experience period varied, and the number of executives, those who received education for public health nurses at university, and those who worked for prefectural health institutions was 18 (15.5%), 19 (16.4%), and 35 (30.2%), respectively, showing no difference between the 3 groups.

In comparison of the groups regarding the scores of all subscales and total scores for expertise, Group A showed significantly higher scores than Groups B and C ($p < 0.001$, $p < 0.01$, $p < 0.05$) (Table 2). Regarding the scale of skills, the score of interpersonal health care skills in Group A was significantly higher than that of Groups B and C ($p < 0.01$), while total skill score of Group A tended to be higher than that of Group B ($p < 0.1$). Regarding the scale of operation, Group B showed a significantly higher score than Group C ($p < 0.01$).

The number of those who answered that an operation system would be established at their institutions within the coming year was 29 (25.0%), including 14 (37.8%) in Group A, and a tendency towards significance ($p < 0.10$) was observed in the χ^2 test. Table 3 presents the institutions that indicated that their operation system would be established within the coming year. For example, they described, "We explained how to use the EPDS to all the health professionals in our institution so that they would be able to use it," "We have used the EPDS and the MABS on postpartum day 5 and 1 month after child birth. We are planning to add the

Table 1. Demographic data

		A (n = 37)	B (n = 40)	C (n = 39)	Total (n = 116)	p [1)]	A' (n = 21)
Personal characteristics							
Age		41.1 (± 9.1)	37.3 (± 7.3)	41.0 (± 8.7)	39.7 (± 8.5)	*ns*	40.65 (± 8.0)
Sex	Male	1 (2.7)	0 (0.0)	0 (0.0)	1 (0.9)	*ns*	1 (4.8)
	Female	35 (94.6)	40 (100.0)	39 (100.0)	114 (98.3)		20 (95.2)
	Missing	1 (2.7)	0 (0.0)	0 (0.0)	1 (0.9)		0 (0.0)
Type of qualification	Public health nurse	30 (81.1)	38 (95.0)	32 (82.1)	100 (86.2)	*ns*	19 (90.5)
	Midwife	5 (13.5)	2 (5.0)	5 (12.8)	12 (10.3)		1 (4.8)
	Nurse	1 (2.7)	0 (0.0)	1 (2.6)	2 (1.7)		1 (4.8)
	Physician	0 (0.0)	0 (0.0)	1 (2.6)	1 (0.9)		0 (0.0)
	Missing	1 (2.7)	0 (0.0)	0 (0.0)	1 (0.9)		0 (0.0)
Years of experience	5 years or less	6 (16.2)	8 (20.0)	5 (12.8)	19 (16.4)	*ns*	4 (19.0)
	6 - 10	2 (5.4)	8 (20.0)	6 (15.4)	16 (13.8)		0 (0.0)
	11 - 15	5 (13.5)	7 (17.5)	12 (30.8)	24 (20.7)		3 (14.3)
	16 - 20	14 (37.8)	9 (22.5)	7 (17.9)	30 (25.9)		8 (38.1)
	21 - 25	5 (13.5)	6 (15.0)	4 (10.3)	15 (12.9)		5 (23.8)
	26 - 30	3 (8.1)	1 (2.5)	3 (7.7)	7 (6.0)		1 (4.8)
	31 - 35	1 (2.7)	1 (2.5)	2 (5.1)	4 (3.4)		0 (0.0)
	36 years or more	1 (2.7)	0 (0.0)	0 (0.0)	1 (0.9)		0 (0.0)
Management position	With title	5 (13.5)	6 (15.0)	7 (17.9)	18 (15.5)	*ns*	2 (9.5)
	Without title	32 (86.5)	34 (85.0)	32 (82.1)	98 (84.5)		19 (90.5)
Education (for PHN)	University	6 (16.2)	8 (20.0)	5 (12.8)	19 (16.4)	*ns*	3 (14.3)
	Other	28 (75.7)	32 (80.0)	31 (79.5)	91 (78.4)		16 (76.2)
	Missing	3 (8.1)	0 (0.0)	3 (7.7)	6 (5.2)		2 (9.5)
Education level	University/graduate school	6 (16.2)	12 (30.0)	6 (15.4)	24 (20.7)	*ns*	3 (14.3)
	Other	27 (73.0)	27 (67.5)	31 (79.5)	85 (73.3)		16 (76.2)
	Missing	4 (10.8)	1 (2.5)	2 (5.1)	7 (6.0)		2 (9.5)
Characteristics of institutions							
Type of institutions	Prefectural health institutions	13 (35.1)	15 (37.5)	7 (17.9)	35 (30.2)	*ns*	8 (38.1)
	Other	24 (64.9)	25 (62.5)	32 (82.1)	81 (69.8)		13 (61.9)

[1)] p value based on χ^2 analysis, Fisher's exact test, or ANOVA; *ns:* indicates not significant.

Table 2. Cross-sectional evalualuation after the second seminar

		A (n = 37)	B (n = 40)	C (n = 39)	a)
		Mean (± SD)	Mean (± SD)	Mean (± SD)	
Expertise scale	Total	3.18 (± 0.40)	2.76 (± 0.58)	2.66 (± 0.34)	$1^{***}2^{***}$
	1: Knowledge of postnatal mental health	3.24 (± 0.41)	2.92 (± 0.50)	2.88 (± 0.35)	$1^{**}2^{**}$
	2: Knowledge of 3 types of questionnaires	3.32 (± 0.50)	2.84 (± 0.71)	2.69 (± 0.44)	$1^{**}2^{***}$
	3: Knowledge of how to use 3 types of questionnaires to continuous support for mothers	2.72 (± 0.52)	2.36 (± 0.67)	2.24 (± 0.48)	$1^{*}2^{**}$
Skill scale	Total	2.49 (± 0.48)	2.23 (± 0.56)	2.24 (± 0.51)	$1^{\dagger}$
	1: Interpersonal heath care skills	2.68 (± 0.53)	2.29 (± 0.62)	2.28 (± 0.51)	$1^{**}2^{**}$
	2: Skill at formulating measures	2.22 (± 0.56)	2.16 (± 0.60)	2.19 (± 0.61)	
Operation scale	Total	1.56 (± 0.28)	1.67 (± 0.24)	1.47 (± 0.31)	3^{**}

a) After ANOVA, Bonferroni's multiple comparison was used to identify significant differences between paires of groups; 1: diffrence between A and B; 2: diffrence between A and C; 3: diffrence between B and C; †: $p < 0.1$, *: $p < 0.05$, **: $p < 0.01$, ***: $p < 0.001$.

Table 3. Operation system that would be established within the coming year

	Operation system	n
1	Start to use the EPDS or 3 types of questionnaires	5
2	Development of a cooperation system in the community	8
3	Seminar or study meeting for postpartum depression	7
4	Discussion meeting to support mothers with postpartum depression	3
5	Expansion of subjects for home visits	2
6	Group meetings for mothers with postpartum depression	2
7	Exchange program for prenatal and postpartum mothers	1
8	Others	6

check list for postpartum depression and infant abuse," "We requested the budget for system development for early detection and continuous support of postpartum depression. We are scheduled to develop the system in cooperation with the municipalities," "We planned a seminar for postpartum depression in cooperation with the health and welfare centers. We will continue to run the seminar in cooperation with hospitals in and after the next year," "We will hold an exchange program for prenatal and postpartum mothers," "We are aiming to make home visits for all newborns," and "We hold group meetings for mothers with postpartum depression." As mentioned above, the details of their operation varied, for example, from the development of an institution to collaboration with other medical facilities and administrative organs, and from primary to tertiary prevention.

The number of participants in both seminars in 2005 and 2006 was 21 (Group A'). The demographic data of the 21 participants is shown in Table 1. No significant difference was confirmed in their demographic data in comparison with overall participants in the seminar in 2006. When a paired *t*-test was performed regarding the scale of expertise, it was found that the score of expertise 2 in the seminar in 2006 was significantly higher than that in the seminar in 2005 ($p < 0.001$) (Table 4). Regarding the scale of skills, the score of interpersonal health care skills and total score in the seminar in 2006 were significantly higher than those in 2005 ($p < 0.01$ and $p < 0.05$). In addition, the score of operation in 2006 was significantly higher than that in 2005 ($p < 0.05$).

3.2. *Study No. 2*

We obtained responses from 277 prefectural health and welfare centers (collection rate: 70.3%). Among the respondents, 267 (96.4%) were public health nurses. The population in 35.7% of the catchment area of the health and welfare centers was less than 100,000.

For the question regarding the use of the CRSM, 107/261 (40.9%) responded that they used it for support of cases, and 63 (24.1%) responded that they used it for seminars; suggesting that the CRSM was used in nearly half of the areas in the nation (Table 5). For the question regarding whether participants encouraged the use of a designated method for the screening of postnatal mental health of mothers as municipal support, 109/267 (40.8%) health and welfare centers responded that they had no special guidance, and among the health and welfare centers where such guidance had been performed, 78/158 (49.4%) used the 3 questionnaires indicated in the CRSM (Table 5).

4. Discussion

In the study performed in December 2005, it was found that self-evaluation of the participants on expertise was generally high, but low regarding skills, suggesting that the seminar might have no proximal effects on skills (*15*). However, as a result of statistical analysis in which the three groups described above were compared with each other in the results of the questionnaire performed after the seminar in 2006, and the results of the questionnaire in 2006 were compared with those from the previous

Table 4. Longitudinal evaluation in two years

		2005 yr ($n = 21$)	2006 yr ($n = 21$)	p [1)]
		Mean (± SD)	Mean (± SD)	
Expertise scale	Total	3.03 (± 0.44)	3.12 (± 0.40)	
	1: Knowledge of postnatal mental health	3.05 (± 0.50)	3.25 (± 0.41)	
	2: Knowledge of 3 types of questionnaires	3.17 (± 0.46)	3.75 (± 0.54)	***
	3: Knowledge of how to use 3 types of questionnaires to continuous support for mothers	2.63 (± 0.59)	2.73 (± 0.54)	
Skill scale	Total	2.27 (± 0.50)	2.53 (± 0.47)	*
	1: Interpersonal heath care skills	2.43 (± 0.46)	2.75 (± 0.54)	**
	2: Skill at formulating measures	2.07 (± 0.70)	2.22 (± 0.49)	
Operation scale	Total	1.44 (± 0.29)	1.56 (± 0.22)	*

[1)] p value based on paired *t*-test; *: $p < 0.05$, **: $p < 0.01$, ***: $p < 0.001$.

Table 5. Screening methods and use of the CRSM

Methods of screening of postnatal mental Health as municipal support ($n = 267$)	Edinburgh Postnatal Depression Scale (EPDS)	71	19.8%
	Mother's Attachment to Baby Scale (MABS)	15	5.6%
	Three questionnaires used in the CRSM	78	29.2%
	Risk assessment tool of abuse (Osaka/Minamitama)	36	13.5%
	Others	24	8.9%
	No special guidance	109	40.8%
Use of the CRSM ($n = 261$)	Use for seminars	63	24.1%
	Use for support of cases	107	40.9%
	Not used	106	40.6%
	Unknown	48	18.3%

year, it was suggested that the seminar would have effects on not only accumulation of expertise, but also improvement of interpersonal health care skills. Elliott *et al*. utilized a program in which client-centered therapy, *etc*., was taught for ten half-day sessions(7-8 months) (*17*), and Appleby *et al*. utilized a 2-day program for health visitors to teach cognitive behavioral therapy using role play (*20*), and they were able to demonstrate improvement of interpersonal health care skills. In our seminars, we did not teach a specific psychotherapy, and thus the simulation performed through assessment of the paper patient and group discussion on support (the seminar in 2005) and group supervision based on actual cases (the seminar in 2006) were considered to be effective. It might be also effective that the participants from the first seminar experienced various cases in daily practice with their expertise and motivation obtained from the first seminar for a full year, and were able to describe the cases, in which continuous support was terminated, before the seminar in 2006.

In this study, no significant changes were confirmed in the evaluation of personal skills at formulating measures. However, it was shown that budget establishment and formulating measures for related operations were promoted. In the inter-group comparison on the scale of operation, performed in a cross-sectional manner in 2006, the level of operation was highly evaluated for the institutions, in which health professionals other than those who participated in the first seminar participated in the second seminar. In addition, when a question was posed to a participant from one institution in a longitudinal manner, the score of operation in 2006 was higher than that in the previous year. The number of those who responded that operation systems could be established at their institutions within the coming year tended to be large among the participants in both seminars. Although increase in personal skills may not necessarily be linked with the operational level, the possibility that the effects of the seminars might increase awareness of operating officers and entire members of an institution and promote the establishment of an operation system was suggested.

Furthermore, approximately 20% of the participants responded to the question about the use of the CRSM and the 3 types of questionnaires that they did not know the CRSM. Thus, it was suggested that the main branches of prefectural maternal and child health organizations might have another policy, their awareness of perinatal mental health and support for child rearing might be low, and that cooperation between prefectural governments and health and welfare centers might be insufficient. However, approximately 40% of the health and welfare centers responded that they had used the CRSM for support of individual cases. It can be concluded that the use of the CRSM has expanded to half of the areas in Japan in 3 years after its distribution to main branches of maternal and child health organizations.

As the method for mental health screening of postpartum mothers used in the municipalities, the 3 types of questionnaires recommended in the CRSM were used in approximately half of the health and welfare centers that instructed a specific screening method. It is hoped that the level of guidance to municipalities by prefectural health and welfare centers will be increased. The risk markers for infant abuse in the Osaka Method (*21*) and Minamitama Method (*22*) were the main risk markers of child abuse that have been used in Japan. In the CRSM, the relationship between the postpartum mental health of mothers and the risk for infant abuse was explained, and the items of the MABS that indicated the risk for child abuse were specifically instructed. But this is a moderate manual prepared with a focus placed on maternal mental health. As shown by Suzumiya (*23*), it will be important to clearly indicate the part that includes both countermeasures for perinatal mental health and for the prevention of infant abuse.

Limitation and future research

In Study 1, it was considered that the participants in the seminar and their institutions would play an active role in supporting this theme, and especially those who participated in both seminars were likely to be active and favorable towards the seminars. Thus, there is the possibility that the effects of the seminars were evaluated favorably. In addition, it may be possible that the effects were overevaluated because objective markers were not prepared for the evaluation of expertise and skills, and a control group was not established. On the other hand, in Study 2, responses were obtained from more than 70% of all of the prefectural health and welfare centers in Japan, and thus the results are considered to reflect the situation throughout Japan.

It was demonstrated that 1) the interpersonal health care skills of health professionals who participated in the seminar had increased, 2) development of activities for postnatal mental health and support for child rearing had been promoted at individual institutions, and 3) the use of the CRSM had been steadily expanding around the nation.

It will be necessary to evaluate the countermeasures for perinatal mental health and support activity for child rearing at the national level, with a decrease in the incidence of severe postpartum depression and infant abuse considered as the primary outcome.

5. Conclusion

As the last stage of program evaluation, outcome evaluation was performed. It can be said that the seminars performed over the 2 years were effective at improving the expertise and interpersonal health care skills of health professionals. The possibility that the seminars might facilitate the promotion of operation

system establishment at the institutions of the participants was suggested. In addition, it was demonstrated that the effects of this project were expanded to almost half of the nation. To determine the effects on development of postpartum depression and prevention of infant abuse, further monitoring will be necessary.

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Original Article

Household out-of-pocket expenditures on health care in Bangladesh according to Principal Component Analysis (PCA)

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Summary **In Bangladesh, illness results in large out-of-pocket health care expenditures for households. Identifying the components associated with health care expenditures should prove meaningful for future policy formulation in Bangladesh. Thus, the objective of the study was to investigate the overall influence of individual health care costs over data space in a probalistic way using Principal Component Analysis for expenditures incurred due to a recent illness. The study is based on secondary data of the Household Income and Expenditure Survey conducted in 2005 by the Bangladesh Bureau of Statistics. This survey is a nationally representative survey in Bangladesh and its sample includes 8,126 individuals who have incurred health care expenditures in the 30 days prior to the survey. Principal Component Analysis was used to analyze the influence of the factors of health care expenditures in Bangladesh. According to results, 58% of the information on the overall data space confirmed that the cost of medicine is greater than any other factor for health care expenditures. Drug-related health expenditures represented a large component and suggest the need for policies promoting the rational use of drugs. If such strategies are considered and implemented in operational stages, the quality of health care should improve and drug expenditures should substantially decrease.**

Keywords: Out of pocket expenditures, Medicine cost, Illness, Principal Component Analysis, Singular value decomposition

1. Introduction

Heavy reliance on out-of-pocket (OOP) financing of health care expenditures in most developing countries leaves households exposed to the risk of unforeseen expenditures that may absorb a large share of their budget. In many developing countries, governments are facing increasing pressure to improve the efficiency and financial viability of health service delivery systems (*1*). Millions of people around the world are prevented from seeking and obtaining needed care each year because they cannot afford to pay the fees for diagnosis and treatment. This can lead to financial hardship and even impoverishment because people are too ill to work. In addition, many of those who do seek care suffer financial catastrophe and impoverishment as a result of paying these fees in both rich and poor countries. A survey in eighty nine countries covering 89 percent of the world's population found that 150 million people worldwide suffer financial catastrophe annually because they must pay for health services (*2*). Ill health can have a significant economic impact on a household. Such an impact can trigger a spiral of asset depletion, indebtedness, and reductions in essential consumption (*3*). According to the World Health Organization (WHO), one-third of the global population lacks reliable access to needed medicines. The high price of medicines is a key factor in their

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inaccessibility. High prices are particularly burdensome to patients in developing countries, where most of the medicines are paid for OOP by individual patients (*4*). State health services may impose a heavy cost burden on households, especially in developing countries (*5,6*). A study financed by the Commonwealth Fund reported that OOP spending on health care services remains a major source of financial insecurity for people with inadequate health insurance coverage (*7*).

Like many other developing countries, Bangladesh has been exploring how scarce resources can be tapped to co-finance health services. Unequal and uneven geographical distribution of medical health care resources and insufficient health care coverage are two long-standing problems in Bangladesh. Although revenue generation is important for the vitality of health services, effects on utilization and on equity of access to health care must also be considered. The WHO report in 2000 highlighted the fact that the performance of a health system affects peoples' lives and livelihood (*7*). The challenge to a health care system is to make health care equitable and sustainable while efficiently using of resources (*7*). Increased access to health care according to need can promote equity and also achieve efficiency through a reduction in per capita health care costs (*8*). Increasing utilization of health services is the prime goal for Bangladesh, as is true for many developing countries. OOP expenditures constitute the single largest component of total health expenditures in Bangladesh. OOP expenditures particularly involve utilization of health services and purchase of drugs. However, expenditures for transportation to access health services are also part of OOP expenditures. Higher public expenditures and better risk pooling mechanisms have been identified to decrease the share of OOP expenditures. The WHO's Health and Millennium Development Goals indicate that OOP expenditures have a severe impact on increasing the poverty rate in India. The estimate for 1999-2000 was that 3.25% of the total population, or approximately 32.5 million people, plunged into poverty because of health care payments. This figure does not include those who were already poor and have plunged into deeper poverty and also confirms that high expenditures on drugs are one of the main reasons for high OOP payments (*9*). Various kinds of indirect costs such as days, wages, or income lost are not taken into account as part of OOP costs.

Any health expenditures that threaten a household's financial ability to sustain itself are termed "catastrophic" and do not necessarily equate to high health care costs. This definition was in response to the severe problems in financing health services in most developing countries. In the developing world, government health budgets declined in real terms in response to macroeconomic problems at the time while demand for health services increased, partly because of population growth and successful social mobilization (*10*). Households in developed countries were protected from catastrophic spending by adequate health insurance coverage or a tax-funded health system. In developing countries, however, high OOP expenditures, an absence of risk-pooling mechanisms in health financing systems, and high levels of poverty can result in catastrophic health care expenditures (HCE) (*7*). As per WHO estimates, families who spend 50% or more of their non-food expenditures on health care are likely to be impoverished (*11*). In a study on household expenditures in Nepal, the amount of HCE, choice of providers, and reported illness were determined at the same time (*12*). Using the HIES-2005 data, the current study analyzed different factors that affect the determinants of household expenditures and attempted to answer the following question: How much are households currently spending on health care to treat a recent illness?

The objective of the study is to investigate the overall influence of individual factors for health care costs over data space in a probalistic way using Principal Component Analysis (PCA) for expenditures incurred due to a recent illness (30 days prior to the survey).

2. Methods

2.1. *Setting: Study area*

Bangladesh, a South Asian country with a population of approximately 158.6 million, has more than 50% of its people living below the national poverty line (World Bank, statistics for 2007). Though a majority of the population lives in rural areas, the government health care system remains a very minor source of health care there. There is no risk-pooling mechanism in financing health care as of yet. According to the WHO, out of total GDP in 2005, 2.8% was spent on health care. A striking fact is that nearly 88.3% of private expenditures are OOP expenditures (*13,14*). The Directorate of Drug Administration (DDA) under the Ministry of Health & Family Welfare, Government of the People's Republic of Bangladesh, is the country's regulatory authority for drugs. The mission of the DDA is to ensure that the common people have easy access to useful, effective, safe, and good quality essential and other drugs at affordable prices. All matters related to drugs and medicines are regulated in Bangladesh by the Drugs Act of 1940 and subsequent regulations. In addition, the government adopted the National Drug Policy (NDP) in 1982, and the Drugs (Control) Ordinance was promulgated in 1982 to implement it. The ordinance controls the manufacture, import, distribution, sale, pricing, and advertisement of all allopathic drugs and medicines and prohibits the production, sale, and use of non-essentials and unnecessary or less necessary drugs and medicines in the country.

2.2. *Data source*

The data used in this study come from the Household Income & Expenditure Survey (HIES-2005) conducted by the Bangladesh Bureau of Statistics under the Planning Division, Ministry of Planning, Government Of the People's Republic of Bangladesh. The Bangladesh Bureau of Statistics (BBS) conducted the survey in all six divisions using a two-stage stratified random sampling approach under the framework of an Integrated Multipurpose Sample (IMPS). The IMPS design consists of 1,000 Primary Sampling Units (PSUs) throughout the country. There are 640 rural and 360 urban PSUs in the sample. A PSU is defined as two or more continuous enumeration areas (EAs) used in the 2001 Population and Housing Census. Each PSU consists of around 200 households. The current sample included 8,126 individuals who have had HCE 30 days prior to the survey. Using a recall period of 30 days prior to the interview, the survey collected information on past perceived illness (reported morbidity), its severity and treatment, and expenditures for that treatment. From this morbidity data, the current study extracted only OOP expenditures for consultations, Hospital/Clinic visits, Medicine, Tests/studies, Transportation, Tips for treatment, and other expenses (*15*). The data are accessible with the permission of the Bangladesh Bureau of Statistics, Ministry of Planning, Planning Division and the Government of Bangladesh.

2.3. *Principal Component Analysis*

PCA is a technique used to reduce multidimensional data sets to lower dimensions for analysis. It is mostly used as a tool in exploratory data analysis and to make predictive models. The analysis involves the calculation of the eigenvalue decomposition of a data covariance matrix or singular value decomposition (SVD) of a data matrix, usually after mean centering the data for each attribute (*16,17*). The results of a PCA are usually discussed in terms of component scores and loadings. PCA is mathematically defined as an orthogonal linear transformation that transforms the data to a new coordinate system such that the greatest variance by any projection of the data comes to lie on the first coordinate (called the first principal component), the second greatest variance on the second coordinate, and so on (*18*). PCA is theoretically the optimum transform for a given data point in least square terms. It can be used for dimension reduction in a data set by retaining the characteristics of the data set that contribute most to its variance, by keeping lower-order principal components and ignoring higher-order ones (*16*). Such low-order components often contain the "most important" aspects of the data. However, depending on the application this may not always be the case.

PCA is employed here to analyze the influence of the factors for HCE in Bangladesh. SVD is used to implement the PCA. A rigorous approach to HCE analysis must involve a weight characterization of the individual variables in the data. One of the challenges of such analysis is to develop effective ways to analyze global influence of the factors. In addition to a broader utility in analytical methods, SVD and PCA can help to provide such a characterization (*18*). SVD and PCA are common techniques for analysis of multivariate data, and health care cost data are well-suited to analysis using SVD. The HCE of thousands of individuals consist of different factors including medicine costs, hospital costs, and pathology costs. SVD analysis can detect the overall influence of individual cost factors over data space in a probabilistic manner. The intended analysis represents the HCE data with a smaller number of variables and detects the weighting pattern of the factors involved for individual variables.

2.4. *Mathematical formulation of SVD*

In linear algebra, the SVD is an important factorization of a rectangular real or complex matrix, with several applications in data processing and statistics (*4,18*). Two vectors x and y are orthogonal if $x^{\mathrm{T}}y = 0$, where T represents the transcript operation. In two or three-dimensional space this simply means that the vectors are perpendicular. Let X be a square matrix such that its columns are mutually orthogonal vectors of length 1, *i.e.* $x^{\mathrm{T}}x = 1$. Then X is an orthogonal matrix and $X^{\mathrm{T}}X = I$, the identity matrix. To simplify the notation, assume that a matrix $X_{m\times n}$ has at least as many rows as columns $m \geq n$. An SVD of an $m > n$ matrix X is any factorization of the form:

$$X_{m\times n} = (U_{m\times m})\,(S_{m\times n})\,(V^{\mathrm{T}}{}_{n\times n}) \qquad (1.1)$$

where U and V are square matrices, and S is a diagonal matrix. The columns of U are called the left singular vectors, $\{\mathbf{u}_k\}$, and form an orthonormal basis for the rows of the data vector X, so that $\mathbf{u}_i \bullet \mathbf{u}_j = 1$ for $i = j$, and $\mathbf{u}_i \bullet \mathbf{u}_j = 0$ otherwise. The rows of V^{T} contain the elements of the right singular vectors, $\{\mathbf{v}_k\}$, and form an orthonormal basis for the columns of the matrix X. The elements of S are only nonzero on the diagonal and are called the singular values (*18*). Thus, $S = \mathrm{diag}(s_1, s_2, \ldots, s_n)$ and $s_r > 0$ for $1 \leq r \leq n$. By convention, the ordering of the singular vectors is determined by high-to-low sorting of singular values, with the highest singular value in the upper left index of the S matrix (*19*). Note that for a square, symmetric matrix X, SVD is equivalent to diagonalization, or solution, of the eigenvalue problem.

The SVD defined thus has implicitly solved the problems inherent in the PCA definition. First, the SVD decomposes a non-square matrix, thus allowing

direct decomposition of the HCE data in either factors or individual orientation without the need for a covariance matrix. Furthermore, assuming a full SVD, the decomposition of a transposed data matrix can be derived from the SVD of its complimentary representative by the relation: $X^T = VSU^T$, which follows from the relation $S^T = S$. This means that the full SVD decomposition of a matrix in factor orientation can be used to specify an SVD decomposition in individual orientation and vice-versa. Thus, direct SVD decomposition keeps all of the relevant information about the null, row, and column spaces of a data matrix in a compact form (*20*). The major advantage of an SVD over a PCA is that of rank estimation and null-space identification can be identified for both the left and right singular vectors as the space spanned by vectors corresponding to the singular values for which $s_j = 0$, whereas if $s_j \neq 0$, then the corresponding singular vectors $\mathbf{u}_j$ and $\mathbf{v}_j$ are in the range of X which is spanned by the column space of the left and right singular vectors which, in turn, span the row space and column space of the data matrix X.

3. Results

HCE data is arranged as $X = \{x_1, x_2, \ldots, x_j, \ldots, x_n\}$ in an $m \times n$ matrix $X_{m \times n}$, where each vector x_j ($j = 1, 2, \ldots, 7$) represents the expenditures of individuals with respect to the j^{th} factor. Thus, each entry x_{ij} of the X matrix is the amount of expenditures for the i^{th} individual of the j^{th} factor affecting the HCE. The elements of the ith row of X form the n-dimensional vector $\mathbf{h}_i$, which is referred to here as the factor effects of HCE on the i^{th} individual. Alternatively, the elements of the j^{th} column of X form the m-dimensional vector x_j, which is referred to here as the expression profile of the j^{th} factor. Thus, the arrangement of data obviously suits SVD analysis. After SVD of X, the left singular vectors $\{\mathbf{u}_k\}$ represent the principal components for individual expenditures based on the factors. The right singular vectors $\{\mathbf{v}_r\}$ represent the principal components for factors over the whole data space and are termed here as *eigenfactors* $\mathbf{e}_r$. The main goal of this analysis is to investigate the characteristics of the eigenfactors.

As mentioned, HCE data is suited to analysis using SVD/PCA. What follows is some of the analytical results. An obvious question is 'what is the significance of using SVD to analyze HCE data?' The point is to investigate the effects of different factors of HCE over the data. The effects of individual HCE factors could also be measured by simply summing up costs factor-wise over the whole data length. There would be no statistical significance to basing a strong conclusion or recommendation on such analysis. Using SVD revealed clear effects of HCE factors on the available data in a probabilistic manner. The data are arranged in seven columns representing seven HCE factors (*doctor's fees, hospital fees, medicine, check-ups, communication, tips, and other expenses*) and 8,126 rows for individuals. After SVD of data matrix X, the elements of the diagonal of matrix $S_{m \times n}$ represent the relative information (variances), also termed as eigen values, corresponding to the principal components (PCs). The principal components representing the eigenvectors provide some significant information. The plots reveal interesting patterns in the data that may warrant further investigation. The eigen values and their cumulative sums are shown in Figure 1. The patterns of the seven eigenfactors are shown in Figure 2.

As is apparent, the first two eigenfactors represent the higher peak for the third factor (medicine). Also of note is the fact that the cumulative information (variance) corresponding to the first two eigenfactors is about 58% and hence provides the most information on the data space. The weights for the other factors are represented by the other eigenfactor or by a combination of several factors. As is apparent from the eigenfactor space, the most informative data space (corresponding to the first two eigenfactors) is influenced by the third factor (medicine).

The overall weight for the whole data space was computed by summing up the eigenfactor over the number of factors as:

$$\delta_{overall} = \sum_{r=1}^{7} e_r \qquad (2.1)$$

The normalized overall weight as shown in Figure 3 also confirms that the most influential factor over the data space was the third one, *i.e.* medicine costs.

Decomposition also revealed statistical significance.

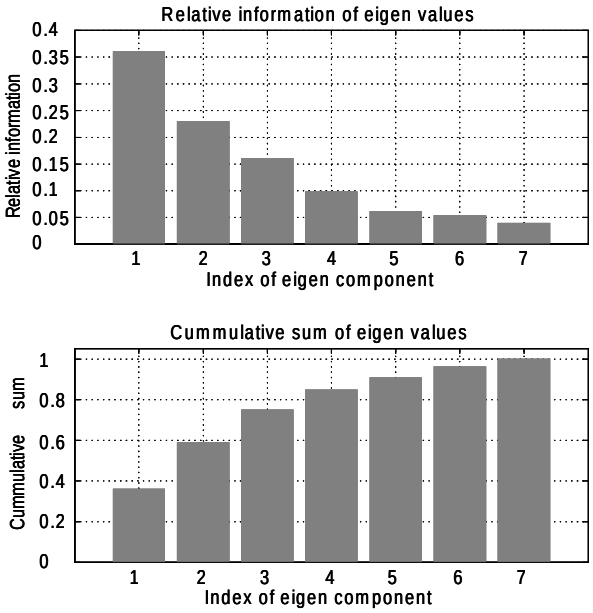

Figure 1. Relative information contained by the eigenvalues (upper) and their relative sum (lower).

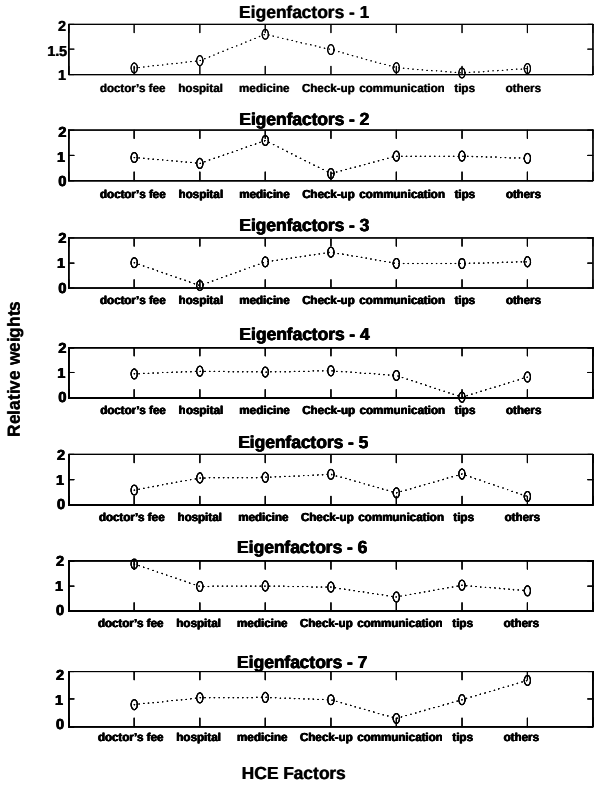

Figure 2. Relative weights of eigenfactors as a function of factors.

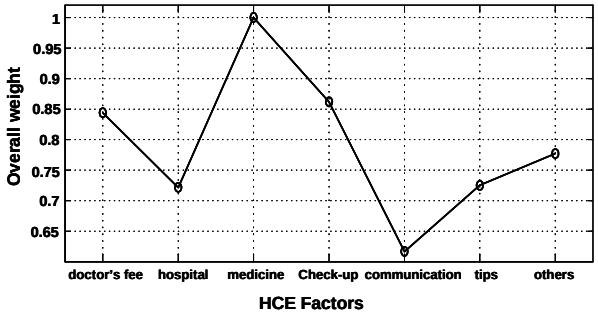

Figure 3. Normalized overall weight as a function of factors.

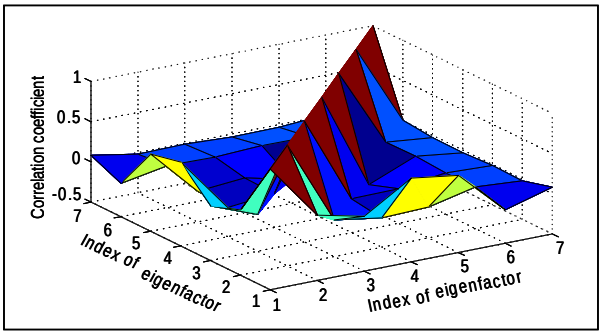

Figure 4. Correlation coefficients among the pairs of eigenfactors.

The correlation coefficient between two eigenfators $\mathbf{e}_a$ and $\mathbf{e}_b$ was defined as:

$$\rho_{ab} = \frac{E\{(e_a - \mu_a)(e_b - \mu_b)\}}{\sigma_a - \sigma_b} \qquad (3.1)$$

where E is the expectation operator, μ_a and μ_b are the expected values, and σ_a and σ_b are the standard deviations of the eigenfactors $\mathbf{e}_a$ and $\mathbf{e}_b$, respectively. The correlation coefficients of each pair of eigenfactors are shown in Figure 4.

As is apparent, the cross terms (correlation coefficients for different eigenfactors) are close to zero, indicating that the eigenfactors are weakly correlated. For many pairs, the coefficients are about zero, which means that both are linearly independent. Consideration of eigenfactors as a basic function with an independent effect on the data space is statistically significant.

4. Discussion

OOP expenditures account for a significant portion of the costs of health care throughout Bangladesh as the country has no risk-pooling mechanism. HCE analysis found that about 58% of the information on the overall data space revealed that the cost of medicine is greater than any other HCE factor. A previous study indicated that unqualified providers (drugstore salespersons and village doctors) and semi-qualified providers together are the major providers of allopathic health care to the poor and disadvantaged in rural Bangladesh, which confirms the present findings of medicine accounting for the highest expenditures. A previous study reported that irrational use of drugs such as over-prescribing, multi-drug prescribing, use of expensive but unnecessary drugs, and overuse of antibiotics and injections are the most common problems in Bangladesh; this also correlates with the present findings (*8,21,22*). However, aggressive marketing by pharmaceuticals companies as well as free availability of 'prescription only' drugs at unlicensed and unregulated drug retail outlets might play a role in the high expenditures on medicine. As these providers have no other channel of information from the formal sectors open to them, they fall easy prey to the marketing strategies of the pharmaceuticals companies (*23*). Because of the fatalistic attitude of the villagers/rural residents, unqualified providers are rarely blamed or held accountable for their poor practices. Due to excessive use of drugs, drug resistance is another problem in Bangladesh. The possible causes of drug resistance are indiscriminate use of drugs by quacks, unqualified personnel, and shopkeepers without training, free sale of drugs from commercial outlets, and a high degree of compliance (*1*). Spending on drugs constitutes the largest share of OOP expenditures on health, drug, and medical supplies and accounts for 79% of total costs in Ghana; similarly, medicine costs represent 64% of the total in Benin (*4*).

Many individuals or factors influence the irrational use of drugs such as patients, prescribers, the workplace

environment, the supply including industry influence, government regulation, and drug information and misinformation. Rational use of drugs in health centers is still a problem in Bangladesh. Reducing the irrational use of drugs at health centers in Bangladesh is not easy, however, since there are numerous constraints such as a lack of resources, lack of knowledge on the part of paramedics, lack of skilled health personnel, low levels of patient knowledge and habits, and demographic constraints. Health is regarded as a human right and the national drug policy promulgated in 1982 was aimed at simplifying the range of drugs available and at improving the logistics of drug distribution at reasonable prices. Given the shortage of qualified health care providers in rural Bangladesh, the importance of unqualified/semi-qualified practitioners as major providers of health care to the poor should be recognized by the public sector, and their capacity should be developed in a planned manner so as to ensure that the poor and the disadvantaged receive an acceptable level of care, at least in the sort term, until supply-side constraints can be alleviated. This will also promote rational use of drugs, improve the quality of health care, and reduce expenditures on drugs. A recent survey evaluating the performance of the latest Health and Population Sector Program (HPSP) in Bangladesh noted that the proportion of people utilizing public health services gradually declined from 13 to 10% and that the proportion seeking unqualified practitioners increased from 50 to 60% from 1999 to 2003 (*24*). The findings of the current analysis reveal greater irrational use of drugs at the household level.

The present study has a number of limitations. First, the study used a cross-sectional design; thus, causality cannot be established. A study using a longitudinal design is necessary to assess the significance and stability of predictors of utilization behavior over time. Second, the study is based on secondary and archival data, which presumably reflects the perspectives and purposes of the original investigators. Shaping the data to match the research questions was a challenge and required an intensive process of understanding the data set, recoding variables, and recasting research variables/questions to match data available. Third, OOP expenditures were recorded for a 30-day period in the surveys and health care spending was based on expenditures reported in that period of 30 days. Fourth, the survey method and the data used in this analysis only partially reveal the situation regarding OOP health care expenditures. Fifth, the HCE components of the survey only include item-specific questions on one broad type of health care services, *i.e.* care associated with a recent illness 30 days prior to the survey. For this type of service, questions were asked on the amounts spent for consultations, medicine, tests, and other expenses. Finally, the survey does not include questions on the types and quantity of medicines prescribed and used. Although the data in this study provides information on household consumption of health care, it only focuses on the collection of OOP health expenditures. Future studies should focus on these issues.

5. Conclusions and Recommendations

Through PCA the current study found that among factors for health care costs medicine costs are a dominant factor in OOP expenditures in Bangladesh. The outcomes of the analysis can be used in policy formulation to improve health system performance in Bangladesh. To promote rational drug use along with a reduction in OOP expenditures at the community level, a greater commitment from drug regulatory authorities, drug manufacturers, and health care professionals is required in order to ensure effective and sound mechanisms of drug management and utilization.

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Original Article

Inhibition of cancer cell growth by anti-Tn monoclonal antibody MLS128

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Summary **Tn-antigens are generally masked by covalently linked carbohydrates but are exposed in most primary and metastatic epithelial malignant tumors, providing sensitive markers for detection of carcinoma. Here, therapeutic potentials of tumor-associated carbohydrate antigen-specific antibodies were investigated. MLS128, an anti-Tn monoclonal antibody, binds to a carbohydrate epitope consisting of three consecutive Tn-antigens (GalNAcα-Ser/Thr). MLS128 treatment significantly inhibited colon and breast cancer cell growth. MLS128 bound to 110-210 kDa glycoproteins on the cell surface. MLS128 treatment caused down-regulation of insulin-like growth factor-I receptor and epidermal growth factor receptor in LS180 colon cancer cells, suggesting that MLS128-inhibited cancer cell growth is in part mediated by down-regulation of growth factor receptors. This study provides the first insights into the potential use of this particular type of anti-Tn antigen antibodies as a cancer therapeutic.**

Keywords: IGF-I receptor down-regulation, Growth inhibition, Colon cancer, Breast cancer, Tn-antigen motif, Antibody therapeutics

1. Introduction

Oncogenic transformation is often associated with dysregulation of glycosylation processes that then leads to altered patterns of carbohydrate functionalization on the surface of cancer cells. Some of these tumor-associated carbohydrate antigens are involved in metastatic processes and are associated with a poor prognosis, thus representing excellent targets for cancer intervention. Tn-antigen (GalNAcα-Ser/Thr) and T-antigen (Galβ1-3GalNAcα-Ser/Thr) are antigens associated with carcinomas and are generally masked by covalently linked terminal carbohydrate moieties in normal human tissues but are exposed in most primary and metastatic epithelial malignant tumors. These epitopes are readily detectable in about 90% of carcinomas and in their metastases, thus providing sensitive and specific markers for pre-clinical detection of carcinoma and for treatment monitoring during and after cancer therapies (*1-4*).

The present study investigated the therapeutic potential of anti-Tn-antigen antibodies using MLS128 that was derived from a mouse immunized with LS180 human colon carcinoma cells (*5*). MLS128 is IgG_3 that recognizes the structure of three consecutive Tn-antigens (Tn3) (*6,7*). This manuscript is the first to describe the inhibition of colon and breast cancer cell growth by MLS128. MLS128 bound to 110-210 kDa glycoproteins on the cancer cell surface. The antibody treatment of LS180 cells caused down-regulation of insulin-like growth factor-I receptor (IGFIR) and

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epidermal growth factor receptor (EGFR), both of which play a critical role in cell growth (*8,9*). MLS128-inhibited cancer cell growth is thus at least in part mediated by growth factor receptor down-regulation. This study provides the basis for the potential development of anti-Tn antigen antibodies as cancer therapeutics.

2. Materials and Methods

2.1. *Materials*

Production and characterization of MLS128 were as previously described (*5,6*). Cell lines used were human colon adenocarcinoma LS180 and HT-29 cells, human breast carcinoma MCF-7 and MDA-MB-231 cells, and human normal mammary epithelial MCF-10A cells, which were obtained from American Tissue Type Culture Collection. Rabbit anti-IGFIRβ antibody and anti-EGFR monoclonal antibody (mAb) were purchased from Cell Signaling Technology (Beverly, MA, USA). Anti-rabbit or -mouse secondary antibody labeled with biotin was from Kirkegaard & Perry Lab. (Gaithersburg, MD, USA). Murine IgG_3 kappa from murine myeloma was purchased from Sigma (St. Louis, MO, USA). Protein G-Sepharose was from Pharmacia Biotech (Uppsala, Sweden). Rabbit anti-insulin receptor (IR) polyclonal antibody (*10*) was used for detection of both α and β subunits of IGFIR because of its cross-reactivity to IGFIR due to sequence homology (*11*). Human placental IGFIR was purified as previously described (*12*). Purified human placental IGFIR was obtained from Beckman Research Institute of the City of Hope, CA, USA.

2.2. *Cell culture*

LS180 cells were cultured in MEM containing 10% fetal calf serum (FBS). HT-29 cells were cultured in McCoy's 5A (Invitrogen, Carlsbad, CA, USA) containing 10% FBS. MCF-7 cells were cultured in IMEM (GIBCO, Gland Island, NY) containing 5% FBS and 11.25 nM insulin. MDA-MB-231 cells were cultured in DMEM supplemented with 10% FBS, 4.5 mg/mL D-glucose, and 110 μg/mL pyruvic acid. MCF-10A cells were cultured in DEME/F-12 (GIBCO, Gland Island, NY) supplemented with 5% FBS, 10 μg/L insulin, 20 pg/mL EGF (St. Louis, MO, USA), and 0.5 μg/mL hydrocortisone. All culture media included 50 units/mL of penicillin-streptomycin and 0.2% Fungizone.

2.3. *Cancer cell growth*

Effects of MLS128 treatment on colon and breast cancer cell growth were determined by counting cells. Cells (~10^4) were plated in wells of a 96-well plate and cultured in respective medium containing 10% or 5% FBS for 24 h. Cells were then cultured in the medium containing 1% FBS with PBS, 160 nM (25 μg/mL) of MLS128 or control mAb, unless otherwise stated, for 4 days. After 24, 48, 72, and 96 h of culturing, cells were collected from each well by treatment with Trypsin-EDTA (Sigma) for 15 min followed by centrifugation at 190 × g for 10 min. Cell pellets were suspended in 0.04% Trypan blue (Sigma). Live cells were counted using a hemocytometer. Triplicate wells were prepared for each data point.

2.4. *Binding of MLS128 to colon and breast cancer cells*

Binding of MLS128 to LS180, HT-29, and MCF-7 cells was measured with the fluorescence activated cell sorting (FACS) Calibur HG (Becton Dickinson, Franklin Lakes, NJ, USA). Cell suspensions (2×10^5 per tube) were prepared, washed twice with ice-cold PBS containing 1% FBS, and incubated with 200 μL of the antibody solution (5 μg/mL or 25 μg/mL in PBS) for 30 min at 4°C. After cells were washed twice with the same buffer, they were incubated with 200 μL of goat anti-mouse IgG (H+L)-RPE (Southern Biotechnology, Birmingham, AL, USA) for 30 min at 4°C. After cells were washed twice with PBS, they were suspended in 400 μL of PBS for FACS analyses.

2.5. *Western blotting analyses of soluble plasma membranes*

Cells (~10^7) collected by centrifugation and washed twice with ice-cold PBS were suspended in 750 μL of 20 mM Tris-HCl buffer, pH 7.5, containing 1 mM EDTA, 1 mM DTT, 1 mM PMSF, and Protease Inhibitor Cocktail (Sigma) (Buffer A); they were then disrupted by passing them through a syringe with a 23-gauge needle 10 times. Supernatants of cell homogenates after centrifugation at 200 × g for 10 min were subjected to centrifugation at 12,000 × g for 30 min. Pellets were solubilized in 100 μL of Buffer A containing 1% NP-40 by rotation for 1 h at 4°C. Soluble membrane fractions were recovered by centrifugation at 12,000 × g for 10 min.

Solubilized membrane proteins were separated by sodium dodecyl sulfate-polyacrylamide gel electrophoresis (SDS-PAGE) on a 6.5% gel and transferred to Immobilon-P transfer membranes (Millipore Co., Bedford, MA, USA). The membrane was blocked with 5% skim milk in TBS for 1 h at room temperature. After incubation with MLS128 (6.25 μg/mL) for 2 h, bound MLS128 was detected using biotin-labeled secondary antibodies, the Vectastain ABC-AmP™ kit, and the Vector substrate kit (Vector Lab., Inc., Burlingame, CA, USA) as previously described (*13*).

2.6. *Lysis and immunoblotting of MLS128-treated LS180 cells*

Cells were washed three times with ice-cold PBS and lysed in 50 μL of TNESV lysis buffer (50 mM Tris-

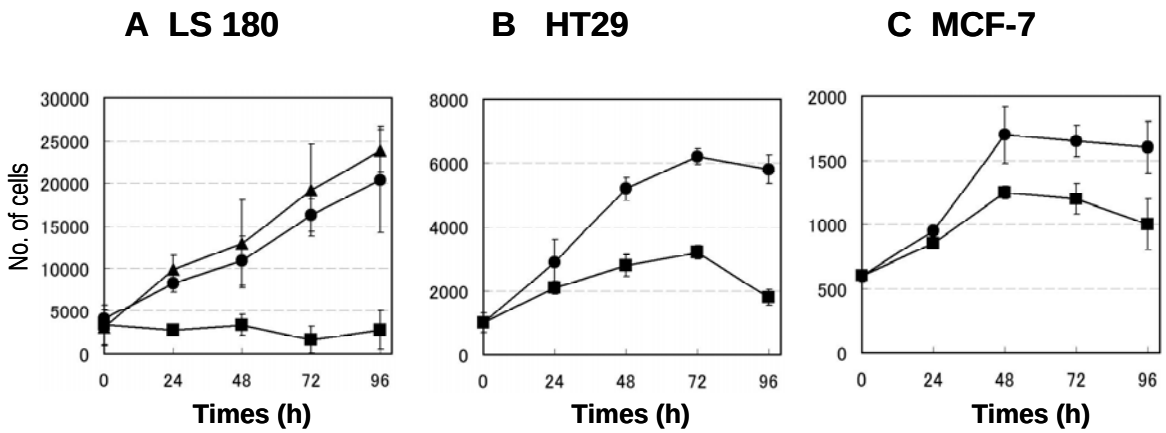

Figure 1. **Effects of MLS128 on human colon and breast cancer growth.** Time course of LS 180 cancer cell growth (**A**) without (PBS: ●) or with 25 μg/mL of control IgG_3 (▲) or MLS128 (■). HT-29 (**B**) and MCF-7 (**C**) cancer cell growth without (PBS: ●) or with 25 μg/mL of MLS128 (■).

HCl, pH 7.4, 1% NP40; 2 mM EDTA; 100 mM NaCl, 10 mM sodium orthovanadate, 1 mM PMSF, 20 μg/mL leupeptin, and 20 μg/mL aprotinin) per 3.5-cm dish. Lysates were clarified by centrifugation at 12,000 × g for 20 min at 4°C. Soluble cellular proteins were subjected to SDS-PAGE followed by Western blotting with anti-IGFIR or -EGFR antibodies.

3. Results

3.1. *Effects of MLS128 on cancer cell growth*

The growth of LS180 colon cancer cells incubated with 25 μg/mL of MLS128 for 24-96 h was inhibited while LS180 cells treated with 25 μg/mL of a control IgG_3 or PBS steadily grew (Figure 1A). To examine whether or not such growth inhibition can be seen with cancer cells other than LS180, time-course experiments similar to Figure 1A were carried out. As is apparent from Figures 1B and C, the growth of HT-29 colon cancer cells and MCF-7 breast cancer cells, respectively, was also significantly inhibited. Thus, the effect MLS128 had on LS180 cells should also take place in other cancer cell lines bearing MLS128-reactive cell surface glycoproteins.

3.2. *Binding of MLS128 with a variety of cancer cell lines*

The binding of MLS128 to cell surface antigens of LS180 cells as well as HT-29 and MCF-7 cells was confirmed by FACS as shown in Figures 2A, B, and C, respectively.

Western blotting analyses of plasma membranes prepared from various cancer cell lines revealed that MLS128 recognized proteins with ~110 kDa in various human carcinoma cell lines including LS180 and HT-29 colon cancer cells (Figure 2D, lanes 1 and 2, respectively) as well as PC-3 and Hep G2 cells (data not shown), whereas 150~200 kDa protein bands were detected in MCF-7 and MDA-MD-231 breast cancer cells as well as HT-29 cells (Figure 2D, lanes 3, 5, and 2, respectively). In contrast, bands reactive to MLS128 were not detected in a normal breast epithelial cell line, MCF-10A (Figure 2D, lane 4). The 125, 75, and 73 kDa proteins detected are endogenous biotin-containing enzymes that were unavoidably stained by the immunoblotting procedure used (*14*).

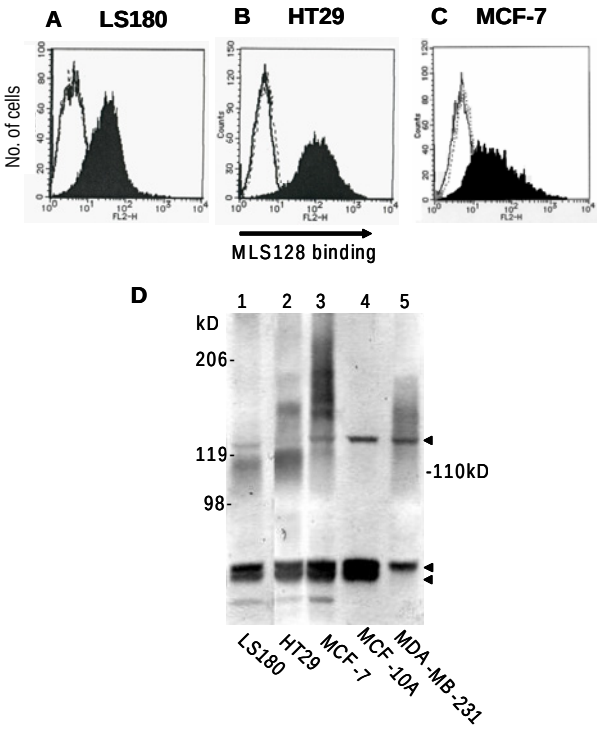

Figure 2. **Binding of MLS128 to cancer cells or solubilized glycoproteins.** MLS128 binding to LS180 (**A**), HT-29 (**B**), and MCF-7 (**C**) cancer cells was measured by FACS as described in Materials and Methods. In **D**, solubilized plasma membranes prepared from various cancer cell lines, *i.e.* LS180 (lane 1), HT-29 (lane 2), MCF-7 (lane 3), MCF-10A (lane 4), and MDA-MB-231 (lane 5), were subjected to SDS-PAGE and immunoblotting with MLS128 as described in Materials and Methods. Molecular markers and the 110 kDa GP are indicated. The 125, 75, and 73 kDa proteins marked with a triangle (◀) are endogenous biotin-containing enzymes (*14*).

3.3. *Down-regulation of receptors for IGF-I and EGF by MLS128 in LS180 cells*

Next investigated was whether or not the expression levels of growth factor receptors such as IGFIR or

EGFR changed after MLS128 treatment of LS180 cells. IGFIR was specifically examined since a number of previous studies found that IGFIR plays a critical role in cell growth and apoptosis (*15*) and since the current authors have shown that anti-IGFIR antibodies inhibit breast cancer growth by down-regulation of IGFIR (*16-18*). Cell lysates were prepared from LS180 cells treated with MLS128 or PBS for 24, 48, and 72 h, and subjected to Western blotting with antibodies for growth factor receptors. The receptor amounts were quantitated by normalization with 73-75 kDa biotin-containing enzymes as internal controls (*14*), and this clearly showed that MLS128 caused down-regulation of both IGFIR and EGFR (Figures 3A and B, respectively).

The 110 kDa glycoproteins (GP) that were identified as MLS128 binding sites on the LS180 cell surface appear to have sizes from those of β (95 kDa) to IGFIR α (130 kDa) subunits. To verify that the 110 kDa GP is not either of the IGFIR subunits, LS180 cell lysates and purified human placental IGFIR were applied to a SDS-PAGE gel side-by-side in triplicate and immunoblotted with MLS128, anti-IGFIR β subunit polyclonal antibody, or anti-IR polyclonal antibody that are IGFIR-cross-reactive due to > 50% amino acid sequence identity (*11*) (Figures 4A, B, and C, respectively). As shown in Figure 4B, the β subunit of IGFIR in LS180 cell lysates and the purified IGFIR was immunostained with the anti-IGFIR β subunit antibody that was used throughout this study. Both α and β subunits of the purified IGFIR were distinctly stained with the IGFIR-cross-reactive anti-IR polyclonal antibody (Figure 4C, lane 2) whereas those of the LS180 lysates were barely stained (Figure 4C, lane 1), indicating that although the α and β subunits of the purified IGFIR loaded onto the gel were much more abundant than those in LS180 lysates, neither α nor β subunits of the purified IGFIR bound to MLS128 (Figure 4A, lane 2) , while the 110 kDa GP in LS180 cells was immunostained with MLS128. These results clearly indicate that the 110 kDa GP is not the IGFIR subunit and that human IGFIR does not contain MLS128-reactive Tn3 epitopes. In summary, MLS128 binding to the 110 kDa GP on LS180 cell surface induces growth inhibition at least in part through IGFIR and EGFR down-regulation *via* an as yet unknown mechanism (Figure 5).

4. Discussion

The present study demonstrated that MLS128 inhibits the growth of not only LS180 cancer cells but also

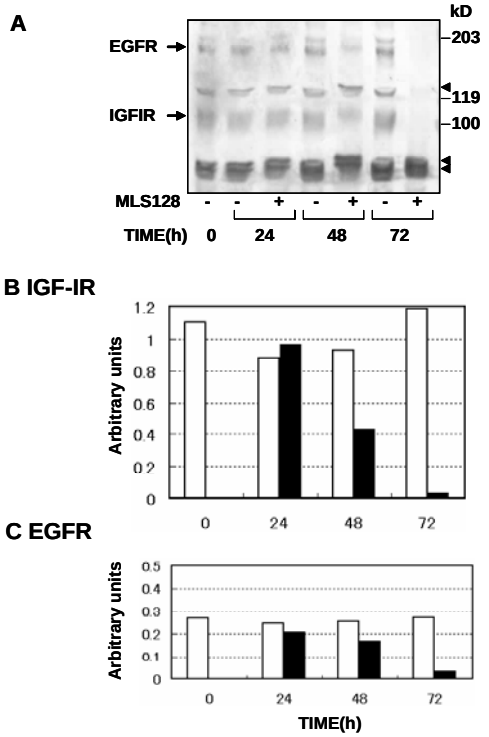

Figure 3. Down-regulation of IGFIR and EGFR in LS180 cells after MLS128 treatment. LS180 cells were treated with MLS128 (25 μg/mL) for the indicated time. Cell lysates were prepared from live cells and subjected to SDS-PAGE followed by immunoblotting with anti-IGFIR β subunit antibody and anti-EGFR (**A**). The 125, 75, and 73 kDa proteins marked with a triangle (◀) are endogenous biotin-containing enzymes (*14*). The amounts of IGFIR β subunits (**B**) and EGFR (**C**) after PBS (□) or MLS128 (■) treatment were estimated by densitometric analysis using the 75 and 73 kDa biotin-containing enzymes (◀) as internal controls.

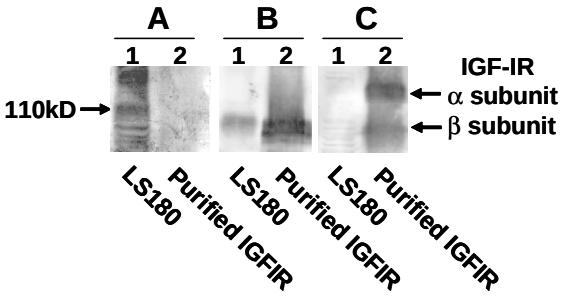

Figure 4. No cross-reactivity of MLS128 to IGFIR. LS180 cell lysates and purified human placental IGFIR were compared in triplicate by immunoblotting with MLS128 (**A**), anti-IGFIR β subunit polyclonal antibody (**B**), and IGFIR-crossreactive anti-IR polyclonal antibody (**C**). The positions for IGFIR α and β subunits as well as 110-kDa MLS128-reactive GP are indicated with arrows.

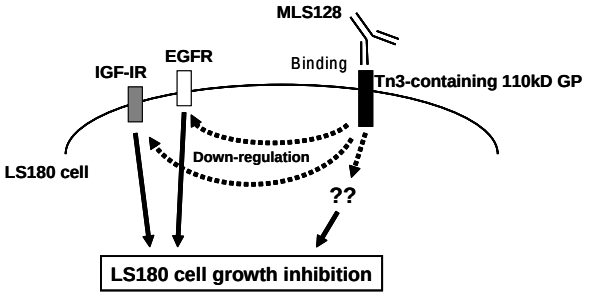

Figure 5. Diagram of MLS128-induced inhibition of LS180 cell growth. MLS128 binding to the 110 kDa GP on LS180 cell surface inhibits growth at least in part through IGFIR and EGFR down-regulation *via* an as yet unknown mechanism.

HT-29 colon and MCF-7 breast cancer cells. During the last two decades, T and Tn epitopes have been extensively studied as cancer-associated carbohydrate antigens, and mAbs to these antigens have been isolated (*1-7*). Immunization with different cancer cells expressing abundant glycoproteins with various Tn-epitopes clearly resulted in the production of Tn3-binding mAbs. Examples of those are, in fact, MLS128 and 83D4, which were isolated from hybridomas generated by immunizing mice with LS180 and MCF-7 cells, respectively (*5-7*).

Avichezer *et al*. previously reported immunoreactivity of mAbs against T and Tn-antigens with human carcinoma cells including ovarian and breast cancer cells (*3*). In their study, however, reduced cell viability of cancer cells was shown after 72 h of incubation at rather high concentrations (~100 μg/mL) of mAbs with unknown epitopes. In contrast, well-characterized MLS128 was chosen for the present study as a first step in evaluating the therapeutic potential of anti-Tn-antigen antibodies. The epitope of MLS128 has been defined as Tn3 (*6,7*). The unique specificity of MLS128 may provide an advantage over other anti-Tn antibodies with a broad range of specificities as reported (*3*) when used in anti-cancer applications. Evaluation of MLS128 binding to a variety of cancer cells should indicate the spectrum of potential applications for future MLS128-based cancer therapy.

MLS128 appears to bind to GPs with ~110 kD on the LS180 cell surface. Immunoreactive species of similar and higher molecular weights were observed with HT-29 and MCF-7 cells. Purification and identification of these glycoproteins is now underway in order to further investigate the mechanisms by which MLS128 inhibits the growth of LS180, HT-29, and MCF-7 cancer cells. Singh *et al*. reported that peanut agglutinin (PNA) bound to cell surface T-antigen expressing glycoproteins of ~110-180 kDa in HT-29 cells (*19*). Their ~110-180 kDa GPs purified with a PNA affinity-column were identified as splice variants of CD44 (CD44v). The MLS128-reactive bands in HT-29 cells detected on the Western blot (Figure 2D, lane 2) resembled those reported as CD44v. Binding of PNA to CD44v, however, stimulates proliferation of HT-29 cells, which is the opposite effect MLS128 has on HT-29 cell growth, thus suggesting that the target glycoproteins for MLS128 on the HT-29 cell surface are not likely to be CD44v. Further study is required to determine which glycoproteins specifically bind to MLS128 and to reveal cellular mechanisms that result in either growth stimulation or inhibition in HT-29 cells.

As far as the mechanisms of growth inhibition in LS180 cells are concerned, this study has provided evidence that both IGFIR and EGFR were down-regulated in LS180 cells after > 48 h of incubation with MLS128. The down-regulation of IGFIR is particularly interesting since IGFIR plays a critical role in cell growth, counteracting apoptosis and tumor transformation (*9,15*). IGFIR down-regulation by anti-IGFIR antibodies has been extensively investigated, which suggests that it is the mechanism for IGFIR antibody-induced inhibition of breast and other cancer cell growth (*17,20*). Unlike previous studies, however, MLS128 in this study caused down-regulation of IGFIR without directly binding to the receptor. Regarding the effect of MLS128 on MCF-7 cells, the IGFIR level did not change after 24-72 h of treatment (data not shown), suggesting that cell growth inhibition by MLS128 is not likely to be mediated by down-regulation of IGFIR in MCF-7 cells.

The present study suggests that MLS128 may be an excellent candidate for development of an anti-cancer therapeutic in addition to its already established diagnostic potential (*21,22*). While this manuscript was in preparation, Ando *et al*. reported that mouse-human chimeric anti-Tn IgG_1 induced anti-tumor activity against Jurkat cells (*23*). Murine anti-Tn mAb KM3413 were isolated by immunizing mice with mucins isolated from LS180 cell culture supernatants, which is a strategy similar to isolation of MLS128. KM3413 has been shown to have affinity for both Tn3- and Tn2-biotin but this affinity is 1/10th of that of MLS128. The presumption is that KM3413 binds to > 100 kDa GPs including CD43 highly expressed in Jurkat cells. Anti-tumor activity by chimeric antibody as was demonstrated in Jurkat-inoculated mice has been shown to be due to the ADCC activity of the human IgG_1 Fc domain. Thus, the mechanism of anti-tumor action of this anti-Tn antibody clearly differs from that of the MLS128 used in the present study. On-going experiments by the current authors also include determination of the inhibitory effects of MLS128 *in vivo*, production of recombinant forms of MLS128, and expression of human single-chain antibodies with affinity for Tn3 (manuscripts in preparation) for further therapeutic development of MLS128-type antibodies.

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Case Report

Case report: Herpes simplex encephalitis in cancer patients

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Summary **The manifestation of herpes simplex encephalitis in patients can often be interpreted as a possible brain tumor. In order to make a definite diagnosis, subsequent invasive testing is frequently required. In addition to other routine diagnostic measures, particular symptoms, especially those indicating that a patient is immunocompromised, should be considered as possible evidence indicating presence of this central nervous system (CNS) viral infection.**

Keywords: Herpes simplex virus, Encephalitis, Brain tumor, Immunocompromised, MRI

1. Case report

A 72 year-old Vietnamese man was presented with a severe headache and fever of 103 degrees. Neurological examination revealed that the patient had minimal left side weakness and mental status changes. Subsequent computer tomography (CT) scan of the head showed a mass effect that extended inferiorly from the sylvian fissure to involve the right temporal lobe with contrast enhancement. Such results were thus interpreted as a possible tumor; hence, the patient was initially treated with antibiotics and steroids. However, the patient showed no response, and to further exacerbate his previous condition, his neurological status began to deteriorate. A follow-up magnetic resonance image (MRI) of the brain, pre and post contrast, showed diffuse involvement of the right temporal lobe with multiple areas of enhancement confined to the region (Figure 1). Additionally, the MRI showed edema and displacement of the uncus into the temporal hiatus. These results led to the consideration of the presence of either encephalitis or brain tumor.

The patient thus underwent a craniotomy with right temporal lobe biopsy and right temporal lobectomy to confirm the diagnoses. Biopsy tissue revealed necrotizing meningoencephalitis as well as lymphocytic infiltration of the meningeal surface and in the brain parenchyma with perivascular distribution (Figure 2A). While there is no evidence of a neoplasm cell, the brain tissue showed further diffuse collections of foamy histiocytes and reactive gliosis indicative of necrosis (Figure 2B). The immunoperoxidase stains further confirmed the Herpes simplex virus I and II with focally positive nuclear staining (Figure 2C). Thus, the histologic and immunohistochemical features are consistent with herpes simplex encephalitis. Post-operatively, the patient developed gastrointestinal bleeding due to the presence of a locally advanced

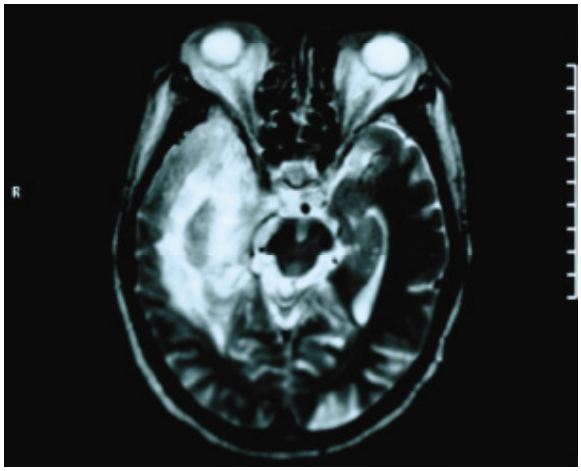

Figure 1. MRI demonstrated right temporal lobe signal enhancement.

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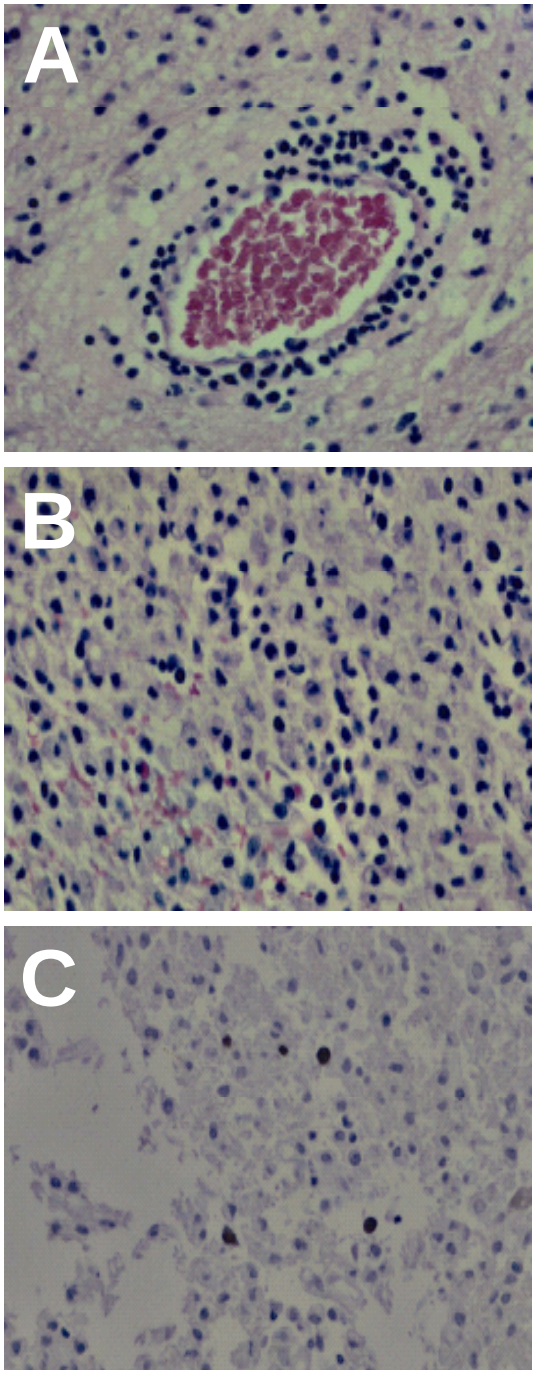

Figure 2. Pathology study of brain biopsy. (A) Biopsy tissue shows necrotizing meningoencephalitis and lymphocytic infiltration on meningeal surface and in brain parenchyma with perivascular distribution. (B) Brain biopsy tissue shows histiocytes and reactive gliosis. (C) Immunoperoxidase stain confirms Herpes Simplex Virus Type I and II with positive nuclear staining.

carcinoma of the sigmoid colon with liver metastasis, confirmed via intraoperative findings. Endoscopic examination further corroborated the presence of a sigmoid colon carcinoma.

2. Discussion

Because this case involves the coexistence of advanced carcinoma with a CNS viral infection, it exemplifies the difficulty of differentiating herpes simplex encephalitis from a brain tumor. Thus, routine tests such as a CT scan or MRI, which are important in delineating the extent of the disease, do not necessarily yield pathognomic findings and are often not enough to confirm either condition (*1*). Laboratory tests such as polymerase chain reaction of the viral genome in cerebrospinal fluid and serum herpes simplex virus antibody measurements are also not definite methods of diagnosing herpes simplex encephalitis; ultimately, a biopsy was necessary to make the diagnosis (*2*,*3*). Worse, polymerase chain reaction results can be confounded with false positive results (*4*). The lack of results and the potential of inaccurate ones only further complicates the diagnosis of encephalitis, cancer, or both.

Herpes simplex virus type 1 encephalitis must also be duly noted in cases with immune-suppressed or compromised patients due to the increased danger and presence of the disease in this demographic. The presence of herpes simplex encephalitis is similar to that of a brain tumor and should be considered in the differential diagnosis, especially in immunocompromised patients with extremely elevated temperatures. Studies have correlated an increased presence of herpes simplex encephalitis in immunocompromised patients (*5*). Furthermore, even in studies with only herpes simplex-susceptible, not immunocompromised, mice, immune response in mere days to fatal herpes simplex virus type 1 revealed brain stem lesions and CNS pathology, which led to fatal encephalitis (*6*). Taken together, it is obvious that the differential of herpes simplex encephalitis be considered early in the treatment of immunosuppressed or compromised patients who have undergone other pertinent diagnostic tests that indicate the possibility of the herpes simplex type 1 virus.

Given the nature of herpes simplex encephalitis, it is absolutely necessary to prioritize its diagnosis if there are any suspicions. Early detection and prompt treatment with an antiviral agent is essential due to high mortality rates (*7*). However, this is encumbered by lengthy and invasive tests and its similarity to brain tumors. Even in non-viral limbic encephalitis devoid of a connection to cancer, it is a challenge to detect CNS antibodies to confirm a diagnosis of encephalitis (*8*). Thus, invasive testing measures are absolutely necessary, not only to confirm potential viral infection but also to ensure the presence or nonexistence of cancer, which may have similar symptoms but different diagnostic results. Thus, thorough invasive testing is the only means of substantially confirming the presence of both conditions.

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