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A systematic review of hepatitis C virus epidemiology in Asia, Australia and Egypt

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Abbreviations
EDHS, egypt demographic and health survey; HCV, hepatitis C virus; HCVPWG, hepatitis C virus projections working group; I-C3, international conquer C coalition; IDU, injection drug use; IV, intravenous; MOH, ministry of health; NGHA, national guard health affairs in Saudi Arabia; NNDSS, national notifiable diseases surveillance system; RNA, ribonucleic acid.

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Abstract

Background: The hepatitis C pandemic has been systematically studied and characterized in North America and Europe, but this important public health problem has not received equivalent attention in other regions. *Aim:* The objective of this systematic review was to characterize hepatitis C virus (HCV) epidemiology in selected countries of Asia, Australia and Egypt, i.e. in a geographical area inhabited by over 40% of the global population. *Methodology:* Data references were identified through indexed journals and non-indexed sources. In this work, 7770 articles were reviewed and 690 were selected based on their relevance. *Results:* We estimated that 49.3–64.0 million adults in Asia, Australia and Egypt are anti-HCV positive. China alone has more HCV infections than all of Europe or the Americas. While most countries had prevalence rates from 1 to 2% we documented several with relatively high prevalence rates, including Egypt (15%), Pakistan (4.7%) and Taiwan (4.4%). Nosocomial infection, blood transfusion (before screening) and injection drug use were identified as common risk factors in the region. Genotype 1 was common in Australia, China, Taiwan and other countries in North Asia, while genotype 6 was found in Vietnam and other Southeast Asian countries. In India and Pakistan genotype 3 was predominant, while genotype 4 was found in Middle Eastern countries such as Egypt, Saudi Arabia and Syria. *Conclusion:* We recommend implementation of surveillance systems to guide effective public health policy that may lead to the eventual curtailment of the spread of this pandemic infection.

The hepatitis C pandemic has been systematically studied and characterized in North America and Europe, but in other areas of the world this important public health problem has not received equivalent attention. The objective of this systematic review is to characterize hepatitis C virus (HCV) epidemiology in Egypt, Australia and selected countries in Asia, i.e. in a geographical area inhabited by over 40% of the global

population. Published studies from the medical literature as well as government or other institutional reports from Australia, China, Egypt, India, Japan, Korea, Pakistan, Saudi Arabia, Syria, Taiwan, Thailand and Vietnam were reviewed in order to provide a comprehensive overview of what is known regarding HCV epidemiology as well as to identify areas that require further investigation and study. By comparing best estimates of regional risk factors and HCV genotype distribution, our aim is to provide an understanding of the current transmission estimates and trends that could be used for projections regarding not only incidence and prevalence but also the overall disease burden, including the ominous complications of HCV infection such as cirrhosis, liver failure and hepatocellular carcinoma. Such an approach will inform health policy, resource allocation and healthcare delivery that may improve to the management of patients with HCV infection.

Methodology

A comprehensive review of the literature was used to gather country-specific data on risk factors, prevalence, number of diagnosed individuals and HCV genotype distribution. References were identified through two sources: indexed journals and non-indexed sources. Indexed articles were found by searching PubMed and regional databases using the following terms: 'hepatitis C AND country name AND (incidence OR prevalence OR mortality OR viraemia OR genotype OR diagnosis OR treatment OR sustained viral response).' Furthermore, references cited within the articles were used. Approximately 7770 abstracts and full articles were reviewed and 690 references were selected based on relevance. In addition, non-indexed sources were identified through searches of individual countries' Ministry Of Health (MOH) websites and international health agency reports. Finally, authors from each country provided government reports and proceedings of local conferences that were not published in the scientific literature. The search included publications in local languages, although reports in English accounted for over 90% of the data sources.

In every case, the prevalence values referred to the prevalence of anti-HCV antibodies that included spontaneously cured and treated/cured individuals. HCV genotype distribution values were based on studies in the viraemic, HCV ribonucleic acid (RNA)-positive, population. Community-based studies were reported, but the focus of this study was to identify/estimate prevalence in the general population. Because the first- and second-generation immunoassay tests provided false-positive results which overestimated the total infected population (1, 2), care was taken to use only studies that used the latest tests to estimate the country's prevalence. In some countries, blood donor data were the main source available for prevalence. The infected general population was composed of high-risk groups [e.g., persons with current or previous history of injection drug use (IDU), dialysis patients and immune compromised persons] as well as non-high-risk groups that contracted the disease through contact with infected blood (e.g. nosocomial infections, dental procedures, etc.). The blood donor population was a good proxy for the latter group. When multiple data sources were available, a systematic process using multi-objective decision analysis was used to rank and select the most appropriate sources (3). When insufficient data were available, data from other countries with similar risk factors and/or population composition were used. Unless indicated, the estimates were for 2004 because of lack of more recent data. When available, subtypes were assessed individually and summed to provide a value for the corresponding genotype. The adult population was defined as ≥ 20 years old.

Results

Australia

In 1998, the Australian Government formed the HCV Projections Working Group (HCVPWG), tasked with estimating incidence and prevalence of HCV (4). Models were developed by this group to estimate prevalence and long-term sequelae of the chronic disease using estimated high-risk populations and incidence of HCV infection. Newly diagnosed, anti-HCV-positive cases were reported to the National Notifiable Diseases Surveillance System (NNDSS) of the Australian Government.

Risk factors

Studies based on NNDSS data showed approximately 80% of infections occurred through IDU (5, 6). Blood transfusions before 1990 accounted for 5–10% of infections in the prevalent population. A study of 800 newly acquired hepatitis C cases reported to NNDSS between 1997 and 2000 found that 93% of all cases with documented risk factors were attributable to IDU, with the trend growing from 84% in 1997 to 95% in 2000 (7). Because transmission via blood supply was virtually eliminated, IDU was identified as the key risk factor along with immigration from endemic countries. Approximately 11% of the infected population were immigrants (8).

Prevalence

A number of publications reported prevalence estimates in the general population (4, 9–13). Studies considered the definitive source for prevalence and incidence were published by HCVPWG (4, 9, 10, 12). Their model considered IDU as well as estimates for infections attributable to immigration and other routes of transmission, such as needlestick injuries in healthcare workers and tattooing. The latest study estimated a prevalent population of 264 000 (all ages) in 2005 (1.3%) with 9700 new infections in the same year. This incidence represented a drop from a peak of 14 000 in 1999 as the result of a reduction in IDU. It was estimated that the total prevalence increased since 1960 and will continue to increase (9, 10).

In a separate analysis, blood samples submitted to all major public and private diagnostic laboratories throughout Australia from 1996 to 1998 were tested as part of a national serological survey for selected infectious diseases (11). Anti-HCV testing in 2800 samples showed an age-standardized prevalence of 2.3%, and a male-to-female ratio of 1.8:1. Peak prevalence occurred in individuals in their 20s to 40s, and the gender ratio was consistent with notifications identified from the NNDSS for the same period. The reported low prevalence in advanced age cohorts was consistent with surveys from England and the USA, all of which identify IDU as the most significant risk factor for HCV (14, 15). Extrapolating to the entire Australian population, 433 000 individuals were estimated to be anti-HCV positive. A number of sampling methodologies were used to minimize selection bias; however, this study most likely overestimated the prevalence as individuals with chronic hepatitis C were oversampled because of their higher utilization of

healthcare services (9). Studies in other subgroups (16–20) and blood donors (21–23) were reported elsewhere.

Diagnosed/incidence

The NNDSS reported the number of diagnosed cases of hepatitis C annually since 1995 (24). Cumulatively, 225 000 individuals were diagnosed and notified through 2005, implying a diagnosis rate of 85% when compared with an overall prevalence of 264 000 in the same year (9, 10). The incidence rates were described above.

Genotype distribution

The published studies were completed 1 year apart and all reported similar results (21, 25–27). A study of 425 patients from a single hospital population reported genotypes 1 (14%), 1a (15%), 1b (23%), 2 (9%), 3 (31%), 4 (5%), 6 (2%) and mixed (1%) (27). The results were consistent with other work conducted by a national reference laboratory (26), which also showed that genotype 3 was more prevalent in younger age cohorts (21–40 year olds), indicative of transmission via IDU, and that genotype 1b was identified more frequently among patients with transfusion-acquired HCV (26).

Summary

The epidemiology of acute and chronic HCV infection has been well characterized by a number of groups including the Australian government (primarily through the National Centre for HIV Epidemiology and Clinical Research) as well as reference laboratories and clinical groups at major tertiary hospitals. The research provided a more complete picture of the epidemic, which is notable for the relatively high proportion of genotype 3-infected individuals compared with other developed countries. IDU continued to be the main driver of HCV infection in Australia. The strength of the population estimates provided a strong basis for future public health planning.

China

HCV has been a notifiable infection in the Hong Kong region of China since 1996; cases are tracked through the Surveillance and Epidemiology Branch of the Centre for Health Protection (28). The use of paid blood donors has been banned in China, but anti-HCV screening reports were not regularly tracked among donation agencies (29).

Risk factors

There were a limited number of risk factor assessments (29–31). A 2009 study on 69 patients from around Anyang found the strongest risk factor to be intravenous (IV) injection, where 75.4% of HCV infections were associated with IV use of glass syringes or needles. A history of blood transfusions was also reported in 73.9% of the cases and was statistically significant after adjustment for other risk factors. An additional significant risk factor was oesophageal balloon use, found in 27.5% of infected individuals. All three risk factors point to under-regulated medical procedures conferring a large risk for HCV transmission (30).

A blood donor study also indicated continued iatrogenic transmission. Risk factor assessments suggested urban, educated individuals who were more likely to see a doctor were at higher risk for HCV, confirming continued transmission in the hospital/medical care-based setting (29).

Prevalence

The estimated HCV prevalence was 1–1.9%. Since 1992, a number of studies reported prevalence within a range of 0.29–9.6% (29, 30, 32–53); however, there were no systematic population-based estimates. Consistent with other countries, blood donor populations provided low prevalence rates because of selection bias. A study in 13 620 volunteer blood donors in one province reported a prevalence of 0.49% in 2003 (29). The prevalence was highest in the 40–49 year olds, at 0.86% (29).

Among non-blood donors, a 1998 study of 3902 individuals from Shenyang province reported a range of 0.42–1.66% (38). Others found a prevalence of 9.6% in 500 elderly individuals (> 55 years of age) in the rural Henan province (32), while Liu *et al.* (30) documented a prevalence of 0.90% in 8226 persons aged 25–65 participating in an endoscopic surveillance study for oesphageal cancer in the Anyang province. In another large study, a prevalence of 1.03% was reported in 12 280 patients admitted to the hospital for a transfusion or other surgical procedure (33).

Diagnosed/incidence

A single incidence study reported a rate of 24.2/100 000 in a sample of 89 647 blood donors in 2007 (54). However, data from other countries suggested that blood donor sampling underestimated the actual incidence rate. Thus, the number of new cases was likely to be higher.

Genotype distribution

Genotype distributions were reported by studies published in 1994–2006 (55–58). A study of 139 HCV patients sampled from nine regions in China (56) reported genotypes 1 (67.6%), 2 (14.4%), 3 (4.3%), 6 (13%) and other (0.7%). Genotype 1b was the most prevalent at 66.2%, and genotype 2a showed a prevalence of 13.7%. Statistically significant geographical differences were observed, and genotype 6 was only observed in the South (56).

A more recent study from Hong Kong sampled 1055 IDUs and non-IDUs in 1998–2004. The non-IDU population showed a genotype 1b prevalence of 63.6%. Genotypes 2a and 3 had prevalence rates of 3.1 and 3.9%, respectively, and genotype 6a was found in 23.6% of participants. The IDU population showed statistically different genotype distributions, where genotype 6a was seen in 58.5% and 1b in 33.0% (55).

Summary

HCV epidemiology in China is largely uncertain. No population-based prevalence or incidence rate estimate is available. Most investigations in HCV have been performed in subgroup studies or voluntary blood donor populations. There is evidence that genotype distribution and prevalence estimates are significantly different across the country, yet prevalence estimates appear relatively low by comparison to other countries in

the Asia Pacific region. Historically, blood transfusions and IV injections appear to be the most prominent risk factors. Additional work is required to better understand the level of existing and new HCV infections in China.

Egypt

The Egypt Demographic and Health Survey (EDHS) reported extensive epidemiological data for the country, including data on HCV knowledge, risk factors and prevalence. The most recent report in 2008 had a sample size of over 12 000 individuals aged 15–59 years, randomly selected throughout the country (59). This study did not distinguish between acute and chronic infections. The blood supply in the country is screened and HCV-infected blood donors are notified.

Risk factors

The EDHS study estimated that 29.6% of anti-HCV antibody positives (25.3% of women and 31.5% of men) received injections to treat schistosomiasis. Additionally, blood transfusion was identified in 24.3% and needle reuse in 20.6% of the HCV-positive cases in this nationwide sample (59). Similar results were described by Frank *et al.* (60). The parenteral injections occurred from the late 1950s to 1980s as the result of a campaign to treat schistosomiasis. In 1969, during the height of this campaign, over 300 000 individuals received IV injections, with an average of eight injections per person in and around the Nile River (60).

Risk factor for new infections were described in a case–control study which found parenteral therapy of schistosomiasis and blood transfusions as risk factors accounting for 13.2 and 9%, respectively, of total infections (61). Invasive hospital procedures and frequent injections were also cited as risks for ongoing transmission. The presence of these factors was seen in over 90% of individuals studied. Nosocomial infection continued to be a risk factor as well. In a study among paediatric oncology patients HCV prevalence was 0.9% at diagnosis, 13.1% after 6 months and 39.6% after cessation of therapy (62). Additionally, familial clustering was noted by multiple authors, suggesting the possibility of household transmission (spouse, father-offspring, sibling transmission) (63–65). Public shaving and IDU were implicated as largely secondary routes of transmission, but these associations were not consistently reproduced (61, 65).

Prevalence

The EDHS report estimated a prevalence of 14.9% for the sampled population of 11 126 aged 15–59 in 2008. Prevalence increased with age, with 55–59 year olds showing a rate of 39.4%. Overall prevalence was 17.4% in males and 12.2% in females (59).

There were a number of studies among blood donors (66–76), and the 2006–2007 studies suggested an overall prevalence in the range of 7.6–8% nationwide (66, 68). Males had a modestly higher infection rate. Prevalence increased with age; 50–59 year olds had the highest prevalence. Rural areas had a higher prevalence than urban (66).

There were a number of studies in subgroups (60, 61, 64, 65, 67, 68, 77–93) and many sampled highly endemic areas, which gave evidence for very high prevalence in select regions (60, 61, 65, 77, 81). A study investigating the differences along the Nile River and its relationship to historical antischistosomiasis treatment in 10–50 year olds found a prevalence of 21.9% (60). A recent estimate among children estimated prevalence of 2% for 1–9 year olds (67). Prevalence was higher in males (11.3%) compared with females (6.5%) in areas along the Nile River (61). Evidence existed that females clear HCV more often than males, which could have accounted for the difference (79).

Diagnosed/incidence

In the EDHS study, 14.9% of the sampled population was anti-HCV-positive and 1.4% was tested positive before this study (59). This implied that 9.4% of the prevalent population had been previously diagnosed before 2008. In 2008, the Egyptian Health Ministry used a national probability sample and reported an incidence of 6.9/1000 persons per year based on regression modeling (94). This estimate is the current gold standard. Other reports calculated 5.2/1000 person years in a study of rural, pregnant women (95).

Genotype distribution

Genotype 4 predominates in Egypt. There are a number of reports (96–98), and a study of 131 HCC and chronic hepatitis C patients found the following genotype distribution: 1 (6%), 3 (1%) and 4 (93% with 4a = 63%) (96).

Summary

Egypt has one of the highest HCV prevalences in the world (nearly 15% of the population). This was caused by repeated IV injections to resolve the schistosomiasis epidemic and transmission through needle reuse. Consequently, the older generations have a higher HCV prevalence than younger ones. Geographically, areas near the Nile River continue to exhibit very high rates of infection. Recent modeling data have also revealed a continuing trend of high incidence rates despite better blood screening measures and better sanitization practices within hospitals. This is in part because of the large reservoir of infected individuals, which increases the potential for continued transmission. Genotype 4 comprises 93% of the total HCV infections, and other genotypes comprise only small proportions of the infected population.

India

There is no national surveillance reporting system in place, and presently the epidemiology is described by isolated studies and blood bank data.

Risk factors

In 2002, the National Blood Policy was created with the hope of creating a unified system to provide a safe and sufficient blood supply for the entire country (99). Despite these efforts, blood transfusion in India carries a higher risk of infection through use of replacement blood donors. While paid donation is illegal, many former paid donors pose as friends or family of patients needing blood (100). In addition, both private and government blood banks are poorly regulated and testing for HCV is viewed as unsatisfactory, in part because of extra costs (100).

A number of studies identified risk factors associated with HCV infection (101–104). Parenteral transmission was

identified as a key risk factor, primarily through exposure in a medical setting. The largest risk factor was blood transfusion, accounting for 38–75% of chronic HCV infections (101, 102, 105). Other risk factors included medical exposures such as the use of reusable glass and traditional syringes (101, 106, 107), which was practiced by as many as 18% of physicians (108). Additionally, haemodialysis and a history of surgery were listed as risk factors (105).

Prevalence

The estimated HCV prevalence was 1–1.9%. A study of 2973 randomly selected individuals in West Bengal determined a prevalence of 0.87% (106). However, this study represented data from one region and blood donor studies showed significant variation between regions. The Northern part of the country had similar practices and risk factors as Pakistan, where prevalence was above 2%. A study of 8130 pregnant women reported a prevalence of 1.03% (109), which is likely to underestimate the prevalence in the general population.

The majority of the reported studies were among blood donors (103, 110–124), with rates ranging from 0.28 to 1.85%. The differences were attributed to different generations of the anti-HCV testing and differences in the populations and practices between different regions of the country (111–113, 117–119, 121). A study of 28 956 mainly male replacement blood donors (family and friends of the patient) in Delhi found a prevalence of 0.66%, which decreased with time from 1.01% in 2000 to 0.29% in 2005 (111). Many of the more recent blood donor studies report prevalence of $< 1.0\%$, indicating that increased screening and education of donors may be working, although testing for anti-HCV is poorly regulated and not always done (110). Replacement donors typically have higher HCV infection rates than voluntary donors (103, 112, 120). Overall, blood donors underestimated the true prevalence because of self-selection.

Studies in high-risk groups found varying prevalence rates. Among IDUs in Northern India, prevalence was 33.7% (125). Haemodialysis patients and thalassaemics receiving multiple blood transfusions showed a prevalence of 41.9 and 25.45% respectively (123). Attendees at a sexually transmitted disease clinic had a prevalence of 2.6% (125). As expected, there was a higher prevalence in those with chronic liver disease with a range of 14–43% (101, 121).

Studies of prevalence by age provided mixed results. One study reported an increased prevalence with age, from 0.31% in individuals < 10 years to 1.85% in those > 60 years, while another found a decrease in prevalence, with the highest rates in adults aged 20–29 years (106, 117). Among volunteer blood donors the highest rate was found in those aged 41–50 (112). Males made up the majority of the study populations in India, but most studies did include some data on females.

Diagnosed/incidence

There were no reported numbers of individuals diagnosed with HCV infection or rate of new infections.

Genotype distribution

The most prevalent genotype was 3, with estimates ranging between 61.8 and 80.2% (101, 102, 104–106, 126–135). A study of 2118 patients across the country found genotypes 1 (31.2% with 1a/b = 92.4%, 1c = 7.6%), 2 (0.5%), 3 (61.8% with 3a/b = 94.9%, 3g/k = 5.1%), 4a/d (4.5%) and 6 (1.9%) (126). They also reported that genotype 3 was most prevalent in the Northern and Eastern regions, while in Western and Southern India the distributions of genotypes 3 and 1 were more even, with genotype 3 between 43 and 52% and genotype 1 between 43 and 48%. A study of 398 patients from North and Central regions also showed genotype 3 as the most common (80.2%), followed by genotype 1 (13.1%) (102). The presence of genotypes 4 and 6 in these populations could indicate a spread from Eastern Asia, where these genotypes are more prevalent.

Summary

There are no studies that measured the general population prevalence across all regions and there appear to be significant variations across the country. Parenteral transmission remains the most significant risk factor, due mainly to IDU and reuse of syringes. Blood transfusion, because of lack of standardized testing and use of replacement donors rather than voluntary donors, remains a potentially large risk factor, and could result in more HCV infections in the general population. Data on newly diagnosed patients are lacking, and more studies are warranted. Genotype 3 is the most common HCV genotype.

Japan

In 2002, a national screening programme was implemented by the Japanese Ministry of Health, Labour and Welfare. This screening programme reports on HCV infection in both high-risk groups and the general population (136). Blood donations have also been screened since 1989 (137).

Risk factors

A 2010 study built on the earlier work of Moriya and colleagues and Yoshizawa and colleagues and commented on the cohort effect evident from multiple sources in the literature (137–139). They identified IV stimulant drug (methamphetamine) abuse among the youth during and after World War II, blood transfusion from paid blood donors, and injections using contaminated syringes and needles, particularly for the treatment of *Schistosoma japonicum* infection, which was endemic in Japan before the introduction of IV antimony in 1921. It was difficult to assign estimates attributable to study designs. The study of 42 young chronic HCV-infected patients identified IDU and exposure during medical procedures as risk factors (137). In a study of pregnant women, 30% of infections were linked to blood transfusions. However, 53% of these individuals were not linked to any particular transmission type (140). An older community-based study of inhabitants suggested that age, blood transfusions and positivity for anti-HBc were all linked to HCV infection (141). Historically, 1/3 of all HCV-positive blood donors were linked to blood transfusions (142).

Prevalence

The estimated HCV prevalence was 1–1.9%. Published estimates come from a large number of blood donor (138, 143–149) and subgroup-based studies throughout the country from 1991 to 2010 (140, 141, 145, 147, 150–184). A study of pregnant women

in 1990–1994 found a prevalence of 0.3% in women < 40, and 1.8% in women over 40, suggestive of the importance of historical risk factors (140). Others showed a 3-year downward trend from 3.9% in 2003 to 3.0% in 2005 in a community-based sample in Osaka, known to contain a high proportion of IDUs (150). In a hospital-based study, 7.1% were HCV positive (152). Further evidence of a large age gradient was reported by other studies as well, with increased prevalence among individuals above 50 and 60 years of age (154, 155).

Blood donor population studies date back to 1990, and all estimated prevalence under 1.1% (138, 143–149). A study of 3 485 648 individuals who donated blood between 1995 and 2000 from eight jurisdictions reported a prevalence of 0.49%, with males and females being almost equal. A Southwest to Northeast gradient of infection was seen, with the highest prevalence in regions located in the Southwest portion of the country. A strong age gradient was also seen: individuals over age 60 were at highest risk for being carriers of HCV (143). Blood donors represented a self-selected population, with the prevalence in the general population always being higher.

Diagnosed population

Studies estimating incidence were scant, although they point to a low incidence. Tanaka *et al.* (185) reported an incidence rate of 1.86/100 000 among blood donors from Hiroshima. Another study reported an incidence range of 1.8–3.4/100 000 (186). On the high end, an incidence of 362/100 000 was reported in a highly prevalent region (156). Diagnosis rate was difficult to determine based on published work.

Genotype distribution

There were a number of publications from 1993 to 2000, and almost all indicated genotype 1b as dominant (158, 159, 171, 187–189). In a 2000 study with 166 samples from an endemic area, the following genotypes were identified: 1b (63%), 2a (25%) and mixed/other (12%) (158). Other studies showed similar results, but further breakout of subtypes (187, 188). The only exception was a study by Kobayashi *et al.* (189), which showed no genotype 1, genotype 2 at 73.3% and genotype 3 at 18.2%. This study was limited to a single hospital located in Tokyo. Except for the latter study, all others showed very small percentages for genotypes 3 and 4.

Summary

Japan can be characterized as a low HCV prevalence country with relatively low incidence numbers, despite a large burden of hepatocellular carcinoma in older populations. Age-specific prevalence rates indicate significant historical transmission routes using unsanitized needles. Regional differences, particularly a Southwest to Northeast prevalence gradient, have been observed and replicated in studies through time. Genotype 1b dominates.

Korea

While a National Health and Nutrition Survey has been in place in South Korea since 1998, it does not yet report on HCV infections (190), and no other general population-based reporting systems have been mentioned in the literature. However, individuals over 40 are suggested to represent a significant portion of infected individuals. In response to this, the Ministry of Health and Welfare and the National Cancer Center initiated an anti-HCV screening programme in 2003 targeted at individuals over 40 (190).

Risk factors

Among existing cases, blood transfusion was reported as the main risk factor (191). However, comparisons between blood transfusions before and after 1992 suggested that there was minimal risk for infection because of transfusion since the start of blood screening in 1991 (191). New infections were therefore arising from other routes of transmission. In a study of 178 infected patients, both previous blood transfusion and a history of endoscopy procedures were found to be associated with HCV infections for patients with genotypes 1b and 2a. Among patients infected with subtypes 1b and 2a, 45.7 and 39.7% were attributed to previous blood transfusions (192). Rural areas reported similar risk factors. In a study of 77 anti-HCV-positive individuals from a rural town in Southeast Korea, blood transfusion before 1992 was found to be significant. Acupuncture was also found to be at risk in this group, with 81.8% of anti-HCV-positive persons reporting this exposure (193).

Injection drug use, which is a key risk factor in other countries, was identified as a potential risk factor. However, this was not thoroughly studied, and therefore further investigation was needed to determine its contribution to incident cases (191).

Prevalence

A prevalence rate of 1.29%, or 193 000 infected-persons aged 40 or older, was estimated in 1995–2000 (191) based on analysis of four large studies with a total sample size of 124 605, where prevalence increased from 0.57% among 40–49 years old to 2.16% among 60+ years old. An earlier study by the author pooled results from 15 reports with a total samples size of 146 561 yielding a prevalence of 1.68% in the general population over 40 years old in 1990–2000 (190). Other studies in 1992–2008 provided a range of 1.00–1.35% (194–196). A much higher prevalence of 5.52% was found among rural volunteers (197).

Prevalence among blood donors decreased since the start of donor blood screening in 1991 (190). In a study done in 1991 of 150 blood donors, 1.30% of individuals were found to be infected (198). More recent blood donor information shows a significant decrease. In 2002–2006, the overall prevalence among blood donors from the Korean Red Cross, hospitals, and for-profit donation centres remained below 0.25%. The decline in prevalence could be because of first generation assays that resulted in false positives, tighter guidelines for blood donation, or an actual decline in prevalence among donors. However, prevalence among blood donors was not representative of prevalence in the general population, as blood donors in Korea were typically young individuals such as students or military recruits (199).

Genotype distribution

There were a few recent studies, with most reports dating back from the 1990s (192, 200–204). The Park *et al.* study (201)

reported the following genotypes: 1 [50.3% with 1a (3.0%) and 1b (47.3%)], 2 [45.0% with 2a (42.6%) and 2b (2.4%)] and mixed/other (4.7%). These findings were consistent with other studies of infected patients, which report subtypes 1b and 2a to be the most frequent (192, 202–204).

Summary

Hepatitis C infection in Korea is a significant problem in older generations, likely because of blood transfusions before screening was implemented. The general population prevalence is about 1.29%, based mainly on investigations of older age groups (40+). In the absence of additional studies, it is unclear what percentage of Korean youth is infected, or if IDU is a significant risk factor for new infections. Genotype 1 is most commonly reported from the current literature.

Pakistan

There is currently no general surveillance or reporting system in Pakistan to track trends in HCV. Owing to the estimated high number of infections, health authorities occasionally run educational campaigns to increase awareness throughout the country, but it is uncertain if these activities are causing a measurable decrease in infections (205). There is also no reporting system in place in transfusion services, therefore data on the safety of the blood supply throughout Pakistan are scarce (206). It is suggested that screening of blood donors for anti-HCV is still insufficient (207).

Risk factors

Pakistan has one of the highest rates of injections by providers in the world. One analysis included 3351 individuals from across the country and identified the following risk factors: reuse of needles or syringes for injections (61.45%), surgeries and dental procedures (10.62%), blood transfusion or blood products (4.26%) and other causes including razor sharing and circumcision by barbers (3.9%) (208). A separate study by the same lead author reported reuse of syringes for antibiotics, vitamins and drugs as the factor most strongly associated with HCV infection in a large study ($n = 6817$) based in Punjab province (209). More than 50% of the cases were acquired in hospitals, pointing to nosocomial infections as the primary source of transmission. Additionally, there was the possibility that public shaving in the male population was a significant transmission route. A large proportion of cases were identified as sporadic, or because of unidentified sources of contamination (209).

A broad, qualitative risk factor assessment based on meta-analyses confirmed the above observations (206). The prevalent exposure pattern was associated with frequent injections for a variety of purposes: intramuscular injections, IV drips used in the summertime to cool down, and prevalent use of injection within the general practice medical setting. A study in the Punjab province indicated smallpox vaccination was associated with HCV transmission (210). Blood transfusions and surgery were also reported as risk factors. A recent case–control survey reassessed anti-HCV prevalence in a volunteer blood donor population, confirming hospital-based transmission through the reuse/multiple use of needles by unqualified providers (211).

Prevalence

A meta-analysis which pooled data from 132 published studies from 1992 to 2008 found prevalence of 3% among blood donors and 4.7% in the general population (212). Similarly, another review of 84 publications using a variety of sampling strategies and subgroups estimated an overall prevalence of 3% in all adults, 2.8% in adult blood donors, 5.4% in adult non-blood donors and 2.1% in children (206). There were geographical differences, as studies from Punjab showed higher rates than the three other provinces, and males had a higher rate of infections than females. Extreme variances existed in Punjab, the largest province, with reported rates upward of 30% HCV positive, which suggested a higher prevalence rate in this region than the rest of the country (206, 209, 212). A 2008 review reported the countrywide prevalence estimate between 2.4 and 6.5% (213).

Blood donor studies typically underestimated the true prevalence because of exclusion of high-risk groups (205, 214–220); however, this was not necessarily the case in Pakistan, consistent with the identified risk factors. Prevalence among blood donors ranged from 0.5 to 8.9%. The largest blood donor study with a sample size of 103 858 was published in 2002 and showed an overall prevalence of 4% (218). Higher rates were observed among rural donors (215) and lower rates were seen among college students (219).

There were a number of studies in subgroups (206, 207, 209, 213, 219, 221–243). A prevalence of 4.57% was reported in 16 400 outpatients in 1998–2002 (232). Higher prevalence among older individuals was seen as consistent across studies of different methodologies and design (206, 208, 209) and higher rates were observed for males over females (232, 241).

Diagnosed/incidence

The incidence and the number of diagnosed patients was largely unknown. From 2002 to 2004, an audit of a single teaching hospital documented an increase in the number of requests for possible HCV positivity. The number of cases, however, appeared to decrease in the same time period from 14.19 to 5.84% (244). This decrease should be taken with caution, as it was based on a single laboratory, and was not likely representative for the country.

Genotype distribution

Genotype distribution information was derived from three studies, which agreed that genotype 3 is the most prevalent genotype (208, 225, 245). The largest study included 3351 individuals from across the county and found the following genotypes: 1 [11.5% with 1a (8.3%) and 1b (3.0%)], 2 [8.4% with 2a (7.5%) and 2b (0.8%)], 3 [67.5% with 3a (49.1%) and 3b (17.7%)] (208). The smaller studies estimate genotype 3 at higher rates of 81.0–86.7% (225, 245), potentially because of the sampling. Similarly, however, genotype 1 was the next most prevalent, showing near agreement among all studies.

Summary

Pakistan has one of the highest HCV infection prevalence rates in the world. Recent work has revealed good estimates in the absence of broad central reporting or a unified data collection

system. The most recent prevalence is estimated at 3%. The Punjab province, in particular, may have a much higher prevalence than the rest of the country. New infections, however, are less certain. The predominance of genotype 3 and the overwhelming role IV injections play in society leaves open the possibility of continued transmission. However, more data on incidence rates are needed.

Saudi Arabia

The HCV infection has been a reportable disease in Saudi Arabia since 1990, although compliance varies. Blood donors are screened and pre-marital testing for HCV has been mandatory since 2007. It is estimated that over one million individuals have already been screened.

Risk factors

Few studies have reported the risk factors in Saudi Arabia. A history of schistosomiasis was found in 7.4% of anti-HCV-positive patients, and prior blood transfusion in 14.8% (246). Another study looked at intrafamilial transmission and found no risk for HCV infection (247). Currently, IDU and blood transfusion are uncommon, indicating other forms of transmission such as bloodletting, traditional tattooing and iatrogenic nosocomial transmission (248, 249).

Prevalence

HCV prevalence was estimated at 1–1.9% among adults. The prevalence in the general population is uncertain given that most studies were conducted more than 10 years ago (246, 250–254). Two studies showed a relatively high prevalence of 5.87% in a cosmopolitan area, and 5.09% in an agricultural region, indicating little difference in urban/rural rates (250, 251).

Although more recent studies among blood donors were available, these studies may not accurately reflect the overall prevalence as they represent healthy adults consisting mostly of males (248, 255–262). Among 557 813 blood donors, a prevalence of 1.1% was reported (259), although two recent studies showed prevalence of 0.6% (255, 258). Older blood donor studies reported higher prevalence rates, likely because of less stringent donation guidelines and no prior testing for anti-HCV (248, 260, 262). However, this higher rate could also be because of a higher prevalence rate among expatriate donors (4.52%) compared with nationals (1.24%) (261).

There were a number of studies in subgroups (253, 254, 257, 259, 263–273). High-risk groups such as haemodialysis patients had a prevalence of 14.7–68% (257, 265, 267, 268, 271, 272). Varying rates were found in the healthy population (5.3%), individuals with a sexually transmitted disease (15.9%), haemodialysis patients (26.1%), thalassemics (33.3%) and haemophiliacs (78.6%), indicating the role of blood transfusion or other nosocomial transmission routes in high-risk groups (254).

Studies reported differences in prevalence with age. In children, the prevalence was reported between 0.1 and 0.9% (259, 273). A general increase in prevalence with age was observed: 4.49% in < 15, 2.05% in 15–24, 5.10% in 25–34, 8.64% in 35–44, 15% in 45–54 and 11.9% in ≥ 55 years old in a cohort of outpatient attendees and admitted patients (250). Others reported that prevalence was highest in males aged > 40 years (6.2%) and in females 40–49 years (5.0%) (246). One study found that in male blood donors, the peak age was 30–39 (260), with similar results from a community-based sample (252). This could indicate that the primary source of transmission in the past was through blood transfusion.

Men made up the majority of the study populations in Saudi Arabia, and had more than twice the rate of women (9.6 vs. 4%) in an outpatient setting (250). However, in a community-based study with equal numbers of men and women, no gender differences were reported (246).

Diagnosed/incidence

HCV infection has been a reportable disease in Saudi Arabia since 1990. Based on data from 2000 to 2005, 37.7/100 000 cases were reported, which included both chronic and acute cases (274). From 1995 to 2005, 24 948 were reported, while in 2007 alone there were 2776 reported cases. Incidence was higher in adults (202/100 000) as compared with children (12/100 000). There were also regional differences—16/100 000 in Jizan to 322/100 000 in Al Baha (275). A study of the population served by the National Guard Health Affairs (NGHA) from 2000 to 2007 found a rate of 78.4/100 000, which may be declining with time (276).

Genotype distribution

Genotype 4 is the most prevalent genotype, followed by genotype 1 (277–282). Among 561 consecutive genotypes performed in a single centre (NGHA) in 2006–2010, the following genotypes were identified: 1 (23.4%), 2 (3.2%), 3 (3.4%), 4 (60.9%) and mixed genotypes, mostly genotypes 4 and 1 (8.7%). Genotype 5 was rare and genotype 6 was non-existent (I. Altraif *et al.*, unpublished data).

Other studies found varying genotypes, where genotype 4 was found in 74% and genotype 1 in 14% (283, 284). In haemodialysis and chronic renal failure patients, infection with genotypes 1 and 4 was almost equally distributed (283, 284). In IDUs, however, genotype 1 was more prevalent (48%), with the majority genotype 1b (39%), followed by genotype 4 (36%) (283).

Summary

The prevalence of HCV infection in Saudi Arabia varies between 0.6 and 1% among blood donors. More recent prevalence studies in the general population across Saudi Arabia are needed in order to get an accurate picture of the current prevalence and risk factors, given that infection by blood transfusion is minimal. There is an increase in prevalence with age, possibly because of varying modes of transmission over time or different risk factor exposures in different age groups. Hepatitis C is a reportable disease in Saudi Arabia, with 37.7 newly diagnosed cases/100 000 inhabitants. In 2007, there were 2776 cases reported. The majority of chronic HCV infections are because of genotype 4, followed by genotype 1.

Syria

There were no reported general population surveillance or screening systems in place in Syria, and epidemiology data were only available from isolated reports in specific populations.

Risk factors

A study among 295 RNA-positive patients aged 2–80 from eight medical centres in 2004–2006 found the following risk factors: blood transfusions or haemodialysis (49%) and tattooing (44%) (285). IDU was identified as a risk factor in only one case (0.3%).

Prevalence

The estimated HCV prevalence was 1–1.9%. While few prevalence studies were published, a study among 2100 predominantly male blood donors reported a prevalence of 0.95% (286). Other studies described much higher rates in specific subgroups. The percent of HCV infected IDUs was similar to other countries at 60.5% (286). Healthcare workers and haemodialysis workers were found to have an infection rate of 3 and 6% respectively (287, 288). However, blood donor studies usually underestimated the HCV prevalence.

Genotype distribution

Genotype 4 was the most common genotype. From a sample of 636 patients from eight medical centres throughout the country, the following genotypes were identified: 1 (28.5%), 2 (0.8%), 3 (1.8%), 4 (59.0%) and 5 (10.1%) (285). On the other hand, a small single-centre study ($n = 37$) found genotype 4 (30%) to be less common than genotype 1 (46%) (289).

Summary

There are few published studies describing the current state of HCV in Syria. From the data available, the prevalence in the general population is likely between 1.0 and 1.9%. However, community studies are needed to investigate true prevalence rates. Healthcare associated parenteral routes such as transfusions and haemodialysis are responsible for about a fifth of infections. The most common genotype is 4.

Taiwan

A national reporting system in Taiwan has not been reported in the literature. However, hepatocellular carcinoma because of HCV infection is a recognized problem in the country and the National Health Insurance programme has funded treatment for HCV since 2003 (290). Taiwan also has one of the most active patient education, awareness and screening programmes in the region funded by companies and individual donors. The Liver Disease Prevention and Treatment Research Foundation was founded in 1994 and initiated screening programmes in 1996. By 2005, approximately 160 000 screenings were performed (291).

Risk factors

Historic high prevalence of hepatitis B in Taiwan has led to a rich literature for both HBV and HCV. One study suggested iatrogenic causes driven by a cultural desire for IV injections for minor conditions and inadequate equipment disinfection (291). Others observed that nosocomial sources were because of past rural medical care being mainly provided by unlicensed practitioners (290). Disposable needles and syringes were not in common use until 1980 (292).

In a study of 272 seropositive men aged 30–64, a negative correlation between anti-HCV seropositivity and education level, a positive correlation with age and a positive correlation with blood transfusions and medical IV injections were found (292). The negative correlation with education was supported by another study which suggested that lower education/lower income persons may delay in seeking medical care, leading to more intrusive procedures (293). A geographical analysis indicated that the age correlation applied only in endemic areas (292). Multivariate analysis was used to analyse risk factors in infected and control groups identifying odds ratio for the following risk factors: blood transfusion (8.6), medical injection (2.4) and acupuncture (2.4). There was no statistically significant correlation for tattooing and haemodialysis, because of too few infected subjects with these risk factors. However, in a study among adolescents, significantly higher rates of anti-HCV prevalence were found among those with a history of transfusion, surgical operation, tattooing, or ear lobe piercing (294). Sun and colleagues examined the HCV genotypes of spousal partners. Most had different genotypes, supporting the conclusions that sexual intercourse was infrequently, if ever, a transmission mechanism for HCV and infections were likely because of exposure to common extrafamilial sources (292).

Prevalence

Using data from the Liver Disease Prevention and Treatment Research Foundation, the HCV prevalence was estimated at 4.4% (or 423 283 anti-HCV-positive carriers) in adults aged ≥ 20 years (291). This study analysed 157 720 subjects in 1996–2005 and found similar infection rates among males and females, an increasing prevalence with age, and significant geographical variation. There were a number of other studies reporting prevalence across Taiwan with a range of 2.9–17.0% (290, 291, 293, 295–298). Geographical variation, with very high endemic regions, was reported by several authors (290–292, 296). For example, Tsai *et al.* (290) reported a prevalence of 2.6–30.9% in townships and 0–90.5% in villages of Tainan county. The prevalence among youth was considerably lower—0% in 3–6 year olds, 0.8% in 7–12 year olds and 1.9% in 13–15 year olds (297, 298). In line with other countries, prevalence among blood donors was considerably lower at 1.2% (299), while haemophiliacs and IDUs had higher rates of infection at 90 and 81% respectively (300).

Diagnosed/incidence

Through active screening, over 300 000 individuals have been screened; however, that accounts for 1.3% of the population. There were no data published on the total diagnosed population. One study did report that in an endemic area, Tzukuan Township, anti-HCV incidence was 4.5% (297).

Genotype distribution

A study of 418 chronic HCV patients at a tertiary referral hospital and another on 1164 patients from three hyperendemic areas found very similar genotype distribution with 1b and 2a being dominant: 1 [48% with 1a (2.6%), 1b (45.5%)], 2 [39.5% with 2a/c (30.9%), and 2b (6.9%)], 3a (1%), 4 (0.2%), 6 (0.5%) and mixed/other (10.0%) (301, 302). It was noted that genotype 1b increased with age, while genotype 2a decreased with age

(302). Other publications reported genotype distribution among students, blood donors and endemic populations (75, 294, 297, 298, 303, 304).

Summary

Taiwan has one of the highest HCV prevalence rates in Northeast Asia, with the highest rates reported in older age groups. This is most likely because of the common use of IV injections for minor conditions, including the inadequate sterilization and reuse of syringes. There is a large geographical variation in HCV prevalence, with certain areas reporting a prevalence of over 30%.

Thailand

To date, there is no national HCV reporting system in Thailand, but blood donors are screened with questionnaires (305).

Risk factors

A study of 214 mostly male patients at a hospital in Northeastern Thailand in 1997–1998 found IDU as the most important risk factor reported in 46.7% of cases, followed by tattoos (32.2%) and blood transfusions (18.8%) (306). Others confirmed the rank order of risk factors in a study of 166 HCV-positive blood donors and found a statistically significant association with previous IDU and transfusion. They also reported an association with multiple sex partners, but this result should be taken with caution as this may be confounded by the presence of multiple risk factors (307).

Prevalence

A study of 5525 persons aged 2–60 across four provinces found a prevalence of 2.15% (aged 2–60) and 2.8% (aged 21–60) in 2004 (305). Prevalence increased with age–1.1% (aged 5–10) to 3.4% (aged 51–60). Interestingly, children aged 2–4 also showed a high prevalence, at nearly 2.1%, indicating the potential for vertical transmission. A separate study of 1534 persons across six provinces found significant geographical variation with a prevalence range of 0.41–2.03% in 2000–2002 (308). There was also evidence of high endemicity (3.8–7.5%) among tribes in Northern Thailand (309, 310). The prevalence among IDU was 86–95% (311–314), while blood donor population prevalence ranged from 0.31 to 3.54%, with higher infection rates among males than females (315, 316). The most recent blood donor study reported a prevalence of 1.37%, and was comprised of voluntary donors from five separate studies (317).

Genotype distribution

An analysis of 45 samples collected in 2004 from four separate regions of Thailand showed genotype 3 as dominant: 1 [33.3% with 1a (6.7%) and 1b (26.7%)], 2c (4.4%), 3 [53.3% with 3a (51.1%) and 3b (2.2%)] and 6 (8.9%) (305). Additional studies sampled blood donors and estimated genotype 3 at 44% of the infected population (318, 319). In contrast, a sample of 46 chronic liver disease patients found genotype 1 as most prevalent. Genotype 1 and its subtypes comprised 48% (320).

Summary

A clear description of HCV in Thailand is largely unavailable, with missing reported data for incidence and diagnosis. IDU appears to be a continuing problem. There are significant geographical variations with very high endemic pockets in the country.

Vietnam

The epidemiology of HCV in Vietnam comes exclusively from isolated studies, as there is no general surveillance system in place. Blood donor screening is not mandatory in the country.

Risk factors

Blood transfusion remained the predominant risk factor, because a large portion of the blood donors in Vietnam were paid and HCV screening was not mandatory (321, 322). It was speculated that the high use of IDU among the donor population was contributing to the increased risk because of blood transfusion. Differences in the prevalence of the disease between North and South Vietnam were also attributed to the longer use of IV drugs by those in the South (323, 324). Tattoos, a history of hospitalization, and occupations other than farmer were also reported as risk factors (325).

Prevalence

HCV prevalence was estimated at 2.0–2.9% among adults. There were considerably different data reported in the literature, ranging from 0.8 to 21% (321–323, 325, 326). Two studies reported prevalence near 0.8% among blood donors in Hanoi and 21% among blood donors in Ho Chi Minh City (321, 323), with higher prevalence among males than females in Ho Chi Minh City. This suggested an increasing prevalence from North to South. A more recent study among 100 individuals in Ho Chi Minh City reported a prevalence of 2% (326). Studies in more rural areas reported a prevalence of 1% (322, 325).

Genotype distribution

The most common HCV genotypes in Vietnam were 1 and 6. There were a number of genotype studies (322, 322, 323, 326, 327). A study in 70 RNA-positive blood donors in Hanoi reported the following genotypes: 1 [47.1% with 1a (30.0%) and 1b (17.1%)], 3 [5.8% with 3a (2.9%) and 3b (2.9%)] and 6 [47.1% with 6a (37.1%), 6e (8.6%) and 6i (1.4%)] (328). Genotype 6 was reported to occur in South China as well as Vietnam, Laos, Thailand and Myanmar (328). In 79 HCV RNA-positive donors from Ho Chi Minh City and four HCV RNA-positive donors from Hanoi, genotype 1 was the predominant genotype (54.0%), composed of genotype 1a (27.0%), 1b (23.0%) and mixed genotype 1 (4%) (323). However, 41% of the genotyped samples were not classifiable into genotypes 1, 2 or 3, and further analysis indicated the majority of the unknown samples were genotype 6a (19.3%) (327). This suggested a geographical distribution of HCV genotypes in Vietnam. Smaller studies reported genotype 1 as the predominant genotype, ranging from 42.8 to 75.0% (322, 326), with the majority typed as genotype 1a (23.8–50.0%), followed by 1b (23.8–25.0%).

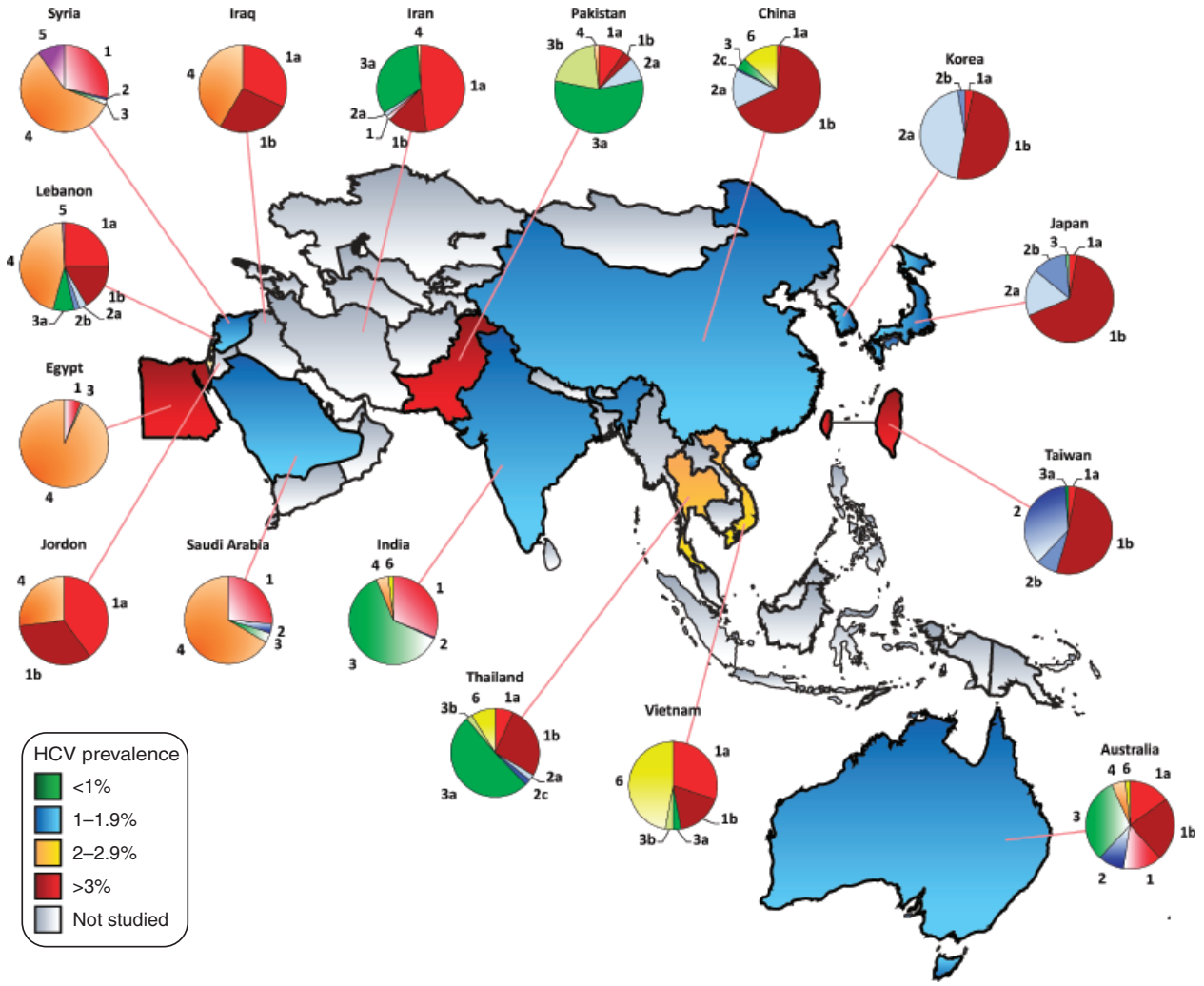

Fig. 1. Hepatitis C virus prevalence among adults and genotype distribution in Asia, Australia and Egypt.

Summary

The prevalence of HCV infection in Vietnam was estimated at 2–2.9%. Additional community studies from both the North and South are needed for a more accurate estimate. Lower prevalence rates are reported in the North, due mainly to less IDU. Blood transfusion remains the predominant risk factor in Vietnam, as almost all blood donors are paid. The most common genotypes are 1 and 6.

Discussion

We estimate that 49.3–64.0 million adults in Asia, Australia and Egypt are anti-HCV positive. This region has the largest population of HCV infected persons with China alone having more HCV infections than all of Europe or the Americas. China (est. 13 million), India (est. 9.5 million) and Egypt (est. 6.5 million) have the highest number of HCV infected persons globally. As expected from such a large geographical and population distribution, there is considerable variability in HCV incidence, prevalence, genotype distribution (Fig. 1) and risk factors (Table 1). While most countries had prevalence rates from 1 to 2%, we documented several with relatively high prevalence rates, including Egypt (15%), Pakistan (4.7%) and Taiwan (4.4%). Even these high overall rates are dwarfed when regional differences within these countries are taken into account. For example, in some populations along the Nile in Egypt, prevalence rates approach 22% and in the Punjab, the most populous province in Pakistan, prevalence rates as high as 30% have been reported. This wide variability in prevalence likely reflects differences in risk factors for acquiring the infection, such as the previous common use of IV injections for the treatment of schistosomiasis in Egypt and the high rate of injections, with reuse of needles and syringes, given for a variety of treatments in Pakistan. Japan has a similar pattern, with nosocomial infection and blood transfusion (before screening) as the most common factors, resulting in the bulk of HCV infection in older patients. Some of these risks are now historical, given changes in immunization and blood transfusion practices. Nonetheless, unique factors in some countries suggest avenues for controlling the spread of infection, although cultural and educational barriers may exist. For example, in Pakistan, where public shaving of beards and other body hair is common and has been identified as a route of

Table 1. Summary of HCV epidemiology data by country

	Top three risk factors	Prevalence rate in adult population	Diagnosis rate
Australia	80% IDU 5–10% Blood transfusion	1.3%	85%
China	75.4% IV use of glass syringes/needles 73.9% Blood transfusion 27.5% oesophageal balloon	1–1.9%	–
Egypt	29.6% Injections for schistosomiasis 24.3% Blood transfusion 20.6% Needle reuse	14.9%	9.4% as of 2008
India	38–75% Blood transfusion Use of reusable glass syringes Nosocomial	1–1.9%	–
Japan	30% Blood transfusion Injections with contaminated syringes/needles IDU among youth	1–1.9%	–
Korea	39.7–45.7% Blood transfusion History of endoscopy Acupuncture	1.3%	–
Pakistan	61.45% Syringe/needle reuse 10.62% Surgery/dental work 4.26% Blood transfusion	4.7%	–
Saudi Arabia	14.8% Blood transfusion 7.4% History of schistosomiasis Bloodletting & traditional tattoos	1–1.9%	–
Syria	49% Blood transfusion or haemodialysis 44% Tattooing 0.3% IDU	1–1.9%	–
Taiwan	76.1% Medical injection 26.8% Blood transfusion 21%Acupuncture	4.4%	1.3%
Thailand	46.7% IDU 32.2% Tattooing 18.8% Blood transfusion	2.8%	–
Vietnam	Blood transfusion IDU Tattooing	2–2.9%	–

HCV, hepatitis C virus; IDU, injection drug use; IV, intravenous.

acquiring HCV and HBV infection, education programmes may help to reduce transmission in future (329). Tattooing in Asian countries is another risk factor which might be addressed via education of at-risk populations (325). Relatively little data are available from these countries on the recently described epidemics of sexually transmitted HCV infection among men who have sex with men compared with that available from Europe and North America; however, the overall prevalence rates appear to be low (330, 331). However, the addition of education programmes regarding the risk of sexually transmitted HCV infection to populations at risk of HIV infection would seem logical.

In addition to the unique risk factors noted above, commonly recognized factors such as IDU will be recognized as widespread in many countries, including Australia, where it is the most common route for acquiring HCV infection. Migration from countries of greater prevalence to those of lower prevalence is likely to result in a general admixture of many different risk factors. Thus, strategies to decrease the spread of HCV infection must include, in addition to the education programmes previously noted, screening of the blood supply before transfusion, avoidance of paid blood donors and, where politically feasible, needle-exchange programmes to decrease the incidence of new infections among IDU populations.

Similar to the large diversity of risk factors, this large geographical region has a great diversity of genotypes. Genotype 1 is common in Australia, China, Taiwan and most countries in North Asia, while genotype 6 is common in Vietnam and other Southeast Asian countries. Genotype 2 is found in substantial proportions, albeit lower than genotype 1, in Japan, Korea and Taiwan. In India and Pakistan genotype 3 predominates, which, because of the very large populations in these two countries, constitutes one of the largest concentrations of people infected with genotype 3 in the world. Middle Eastern countries such as Egypt, Saudi Arabia and Syria predominantly have genotype 4 infection, although genotype 3 can be found in other Middle Eastern countries such as Iraq and Iran, probably related to migration patterns in this area. Genotype 5 occurs in small numbers of patients in Syria but is rarely reported in Asia; similarly, genotype 6 is predominantly in Asia, with the greatest concentration in Vietnam. The clinical significance of this genotype distribution is based in the influence of genotype on response rates to combination therapy with interferon and ribavirin, being greater for genotypes 2 and 3 and lower for

Table 2. Availability and quality of hepatitis C virus (HCV) epidemiology data by country

	Risk factors	Prevalence rate	Genotype distribution	Incidence rate	Diagnosis rate
Australia	*****	***†	****	****	*****
China	**	**	***	**	
Egypt	*****	*****	***	***†	*****
India	***	**	*****		
Japan	***	**	**	**	
Korea	***	***	***		
Pakistan	*****	***	*****		
Saudi Arabia	*	***	***	***	
Syria	***	**	***		
Taiwan	*****	*****	***	*	
Thailand	***	***	**		
Vietnam	*	**	**		

†Australia's prevalence and incidence data is based on a model rather than a general population study. Egypt's incidence is based on a robust model.

Prevalence, risk factors, genotype distribution, diagnosis rate, treatment rate:

*Estimate without a formal study

**Small study in select population (prevalence and diagnosed < 1000; genotype < 100, risk factors < 200) or blood donors study

***Large study in select population (prevalence and diagnosed > 1000; genotype > 100, risk factors > 200)

****Small study in the general population (prevalence and diagnosed < 1000; genotype < 100, risk factors < 200)

*****Large study in the general population (prevalence and diagnosed > 1000; genotype > 100, risk factors > 200)

Incidence:

*Estimate new infections without a formal study

**Incidence study

***Country wide registry-voluntary or with low level of participation

****Country wide registry-manditory or with high level of participation

*****Country wide registry-distinction between new and existing infections

genotypes 1 and 4. Response rates in genotypes 5 and 6 to combination therapy are less well characterized. Combination therapy with interferon and ribavirin is likely to remain the most commonly available treatment in many countries throughout Asia and the Middle East for the medium term, despite the greater availability of the new direct-acting antiviral agents in Europe and North America.

The studies reported here have several limitations, as shown in Table 2. Reliable reports on new infections are rarely available and often there are little data concerning the size of the diagnosed population. There is considerable variability in the type and quality of prevalence studies among the countries assessed. Countries like Australia, Egypt and Taiwan have completed large population studies or developed predictive models, while data from other countries, for example India and China, have relied on studies in subgroups. Over-representation among men in studies from Egypt, Saudi Arabia and Pakistan make estimates for women less certain, although the results of small studies, showing high prevalence rates, have been reported (332).

In summary, the vast population that resides in the area from the Middle East to Oceania presents an extraordinary and wide-ranging, but perhaps not unexpected, variability in the epidemiology of HCV infection. All of the known genotypes have been documented and a diverse range of risk factors for acquiring the infection is evident. The gaps in knowledge are clear and will depend on countries with large populations, such as India, Pakistan and China, continuing to develop high-quality surveillance and reporting programmes. The knowledge gained from such programmes can then be used to develop effective public health policy that may lead to the eventual curtailment of the spread of this pandemic infection.

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