Bovine Brucellosis in Pakistan: Epidemiological Investigations of a Zoonotic Disease

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ABSTRACT

Brucellosis is a major bacterial zoonotic disease with a global distribution. It is mainly a reproductive disease and infected animals are lifelong carriers within the herd. Humans become infected through close contact with livestock and consumption of milk products of infected animals. There is a lack of general awareness of this disease in Pakistan, with little information about the prevalence and disease epidemiology in smallholder settings. Further, dairy animals are critical to the livelihoods of smallholders, and the impact of the disease can seriously affect their economic security as well as their own health. The purpose of this chapter is to examine what is currently known about the epidemiology of brucellosis in Pakistan. After a review of current literature, it describes several studies undertaken as part of a PhD. The first study described is an assessment of diagnostic tools used to detect brucellosis in cattle and buffalos. This information is then used on the next study described, together with a Bayesian statistical method, to estimate prevalence of brucellosis in dairy animals in several districts in Punjab and Sindh provinces. To understand risk factors that may lead to brucellosis in livestock and humans, a 'knowledge attitude practices' (KAP) study is described, coupled with a participatory epidemiology study, which delved into the decision-making processes of male and female farmers in relation to practices which might affect brucellosis transmission. Finally, some implications of these findings are considered, and how an intervention program might be implemented in Pakistan.

Key words: intervention; KAP; prevalence; risk factor; smallholder

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1. INTRODUCTION

Brucellosis is one of the world's major zoonotic diseases. It is considered by the Food and Agriculture Organization (FAO), the World Health Organization (WHO), and The World Organisation for Animal Health (WOAH, formerly the Office International des Epizooties, OIE) as one of the most widespread zoonoses in the world. Brucellosis in animals is predominantly a reproductive disease and causes abortion storms during the breeding season. These bacteria can spread within the herd via contaminated material, such as aborted foetus material and vaginal secretions and urine. *Brucella* pathogens are intercellular and persist within an individual animal, resulting in lifetime carrier status (Ficht 2003). The disease mainly affects sexually mature animals, and causes late-trimester abortions, weak calves, and infertility characterized by placentitis and epididymitis. Infected animals shed the pathogen in uterine discharge and milk (England et al. 2004). Brucellosis transmission typically occurs to other animals through oral contact with aborted foetal material (Bercovich 1998). Brucellosis can be considered to be a disease of animals; however, humans are accidental hosts. The disease in human's results from ingestion or inhalation of the pathogen or direct entrance via skin abrasions. It is also acquired through the consumption of raw milk and its products (Dasari et al. 2013).

Brucellosis is a neglected disease in Pakistan because of a lack of awareness of the disease and the absence of a control program, and its exact prevalence is unknown. Previous studies in Pakistan have focused on determining the prevalence of the disease on large commercial farms (Abubakkar et al. 2011). However, these estimates do not apply to the smallholder system in Pakistan, which comprises 95% of cattle in the country (Afzal 2009). Consequently, there is a need to address this important disease at the smallholder farmer level. It has also been stated that the data about brucellosis in Pakistan are sparse and inconsistent and therefore need to be investigated thoroughly (Munir et al. 2011). In developing countries, dairy animals are critical to the livelihoods of smallholder farmers and the rural poor, hence a great proportion of the Pakistani population may be affected in some way by the disease. Furthermore, in rural areas, the literacy rate is very low (UNESCO 2003) and most farming families have little knowledge about animal diseases. This, coupled with unhygienic practices (Asif et al. 2014), puts them at an even higher risk of contracting the disease if the pathogen is present in animals (WHO 2006). Housing and population density are key factors that have been linked to the progression of diseases and are likely to play a role in the Pakistani system.

This chapter explores various aspects of the epidemiology of bovine brucellosis in Pakistan. After reviewing some information published in the literature, it summarizes some of the key results published as a series of papers from a Ph.D. at Charles Sturt University, Australia, by the first author (Arif et al. 2017; Arif et al. 2018a; Arif et al. 2018b; Arif et al. 2019). In addition, the implications of these results are discussed, together with how the information may be used for an intervention program to control bovine brucellosis in Pakistan.

2. RISK FACTORS FOR BRUCELLOSIS IDENTIFIED IN THE LITERATURE

Brucellosis is an important zoonosis for both developed and developing countries. However, the disease is of more concern in developing countries where there are numerous socio-economic limitations, and factors that contribute towards disease spread, both in animals and humans. Risk factors for animal brucellosis are well documented in the literature, which includes animal age, species, breeding status, herd size, purchasing of new animals, abortion history as well as the herd management practices that contribute to disease transmission between animals. In particular, risk factors specific to developed- and developing-country contexts have also been identified (Hirsh et al. 2004; Lindahl et al. 2014). Recently, a few reports also confirmed these risk factors for bovine brucellosis in Pakistan (Ali et al. 2017).

Human brucellosis is an occupational disease, as people who have close interactions with animals are likely to have a higher risk of contracting the disease, including farmers, butchers, animal health service providers, slaughterhouse workers, and laboratory technicians (Al Shamahy and Wright 2001). Risk factors for human brucellosis are also established and have been described earlier (Lindahl et al. 2015). However, human brucellosis is strongly linked to the environment where people live and the routine practices they use to manage animals. The herd management practices, for example handling animal abortions, consumption of raw milk and its products, assisting animal parturition, and living in a shared place with animals, are known to increase the risk of human brucellosis (Lulu et al. 1988; Corbel 2006; Sofian et al. 2008). Engagement in risky practices for disease transmission varies in different countries and production systems according to the awareness level of the farming communities, animal production systems, and the culture of the region. The association of these practices with disease and with disease awareness among farmers has been investigated in other developing countries (Lindahl et al. 2015). However, risky practices and their association with brucellosis have not been studied in smallholder farming communities in Pakistan. In conclusion, there is a great need to investigate the disease epidemiology in the smallholder production system, to investigate farmers' awareness levels, their perceptions towards risk, disease burden in the study region as well as the best diagnostic approach for the local field conditions.

3. BACKGROUND AND OVERVIEW OF THE APPROACH USED IN THE PRESENT STUDY

Brucellosis is a neglected disease in Pakistan and remains an endemic challenge due to a lack of public awareness and consistent preventive measures. While limited studies have been carried out on large and commercial farms, smallholder dairies, which account for 90% of the dairy industry in Pakistan (Afzal 2009), are neglected. To address this important disease at the smallholder farmer level, the studies described here report on several critical components that are required to enhance understanding of the issue. The first of these is developing a method for the estimation of the prevalence of bovine brucellosis in smallholder farms and the second is the identification of household management practices and herd management practices on smallholder farms that may present a risk for the acquisition of brucellosis from cattle and/or buffalo in humans. Finally, information about the potential for uptake of biosecurity measures by these farmers and their families was obtained, along with the knowledge, perception, and communication networks of farming communities regarding zoonotic diseases. This work provides direction to develop a targeted intervention program that will contribute to the control of brucellosis at the smallholder level. A graphical summary of the approach used in this study is shown in Fig. 1.

4. DIAGNOSTIC TESTS FOR THE DETECTION OF BRUCELLOSIS

Three different diagnostic tests were used in this study, namely the Rose-Bengal test (RBT), competitive ELISA (C-ELISA), and indirect ELISA (I-ELISA). In the absence of a 'gold standard' to detect Brucella infection, a Bayesian latent class analysis (LCA) method (Hui and Walter 1980) was used to evaluate diagnostic test performance in terms of sensitivity (Se) and specificity (Sp), as well as prevalence estimates. However, the evaluation of diagnostic tests reported by Arif et al. (2018a) revealed some discrepancies in the published literature in terms of Se and Sp of RBT. RBT is considered to have a high Se (OIE 2009) and this assumption has been the basis of the use of this test as a screening test rather than a confirmatory test. For example, studies carried out in Zambia and Zimbabwe (Muma et al. 2007; Matope et al. 2011) reported a very high Se (84-99%) but, in contrast, two recent studies (Rahman et al. 2013; Ahasan et al. 2017) reported a very low Se (58-80%) of RBT when used in field conditions in Bangladesh. The research reported in the current study supports these findings with laboratory analyses from several samples testing positive based on the

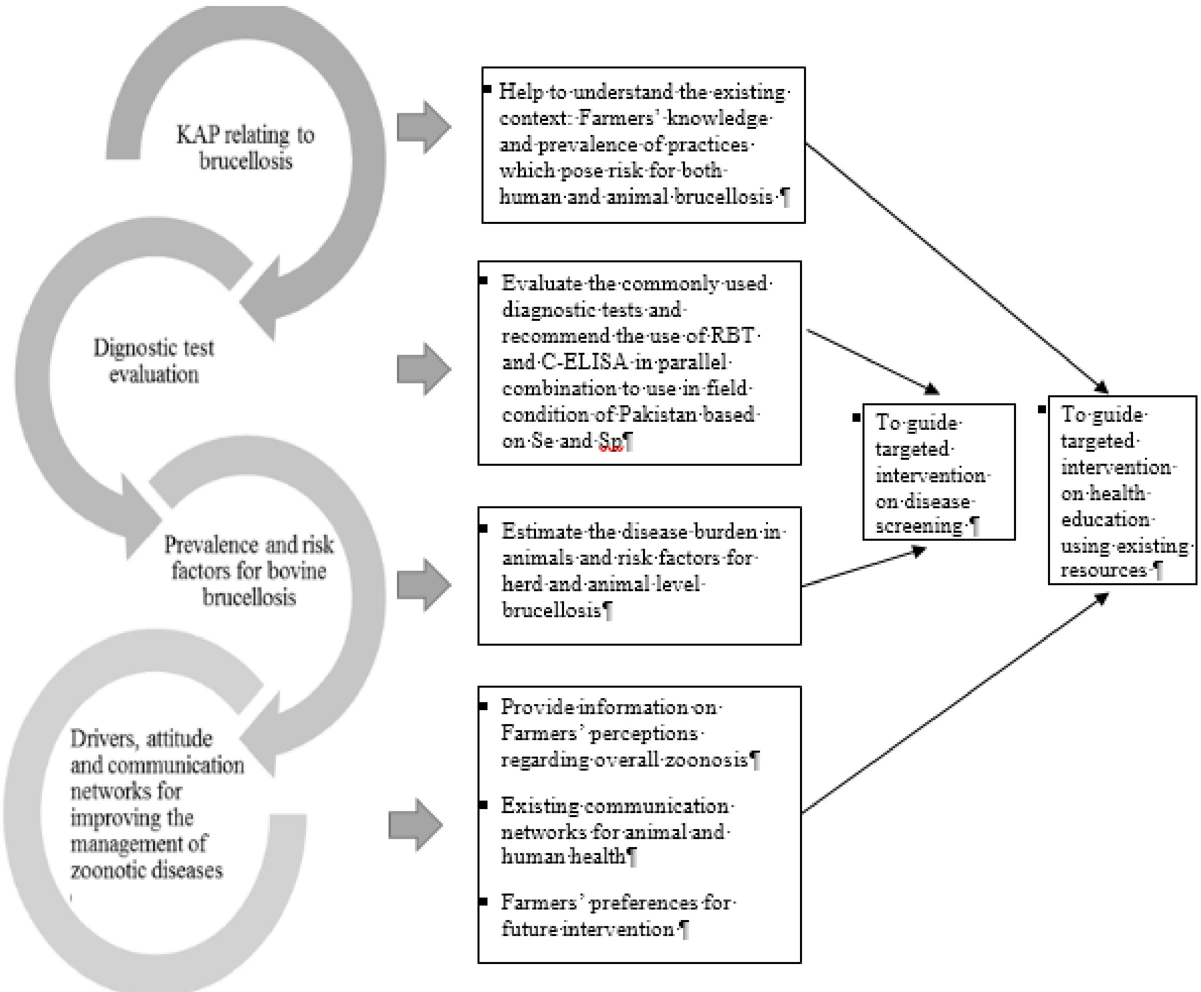

Fig. 1*:* Overarching aims of the project and the potential implications of the work. KAP is 'knowledge, attitudes and practices'

results of ELISA and negative on RBT. Therefore, this evidence raises concerns for the use of RBT as a screening test in field situations in Pakistan, and, to our knowledge, this is the first time that diagnostic tests for brucellosis have been comprehensively evaluated in Pakistani field conditions. The results of the current work indicate that C-ELISA has a higher Se compared to RBT and I-ELISA using LCA. The study also found that the diagnostic tests perform differently in cattle and buffalo and, in general, the Se of all three tests were higher in buffalo compared to cattle. In isolation, C-ELISA performed better than RBT and I-ELISA. A comprehensive sensitivity analysis was also performed using different prior information on Se and Sp from the literature and it was found that the use of minimally informative priors in the LCA produces unbiased results. This approach has the advantage that it allows the tests to be developed purely for the local context, rather than being influenced by test performance in other contexts.

In the smallholder setting, there is a greater cost of a false negative result, leading to undetected cases of brucellosis with health impacts for both animals and humans. Therefore, in this setting, we would prefer to increase the Se at the cost of Sp. Considering this scenario, we also evaluated the Se and Sp of applying the three tests in different serial and parallel combinations. Based on this analysis, RBT and C-ELISA in parallel combination produce the highest negative predictive value (NPV) and reasonable positive predictive value (PPV). This combination is cost-effective as only two tests are required, and not the additional I-ELISA test, and it also provides a better option for herd screening according to the local context. Therefore, this research suggests that none of the three tests evaluated in the current study should be used as a single test in naturally infected animals in Pakistan, as they are not sensitive enough to screen the herd. In the smallholder context, two or more tests are required to screen the herd, with the optimal choice being RBT and C-ELISA in parallel combination.

5. PREVALENCE ESTIMATES OF BOVINE BRUCELLOSIS

The seroprevalence of bovine brucellosis was investigated in seven districts of Pakistan, namely Kasur, Okara, Pakpattan, Jhelum, Bhakkar in Punjab province, and Thatta and Badin in Sindh province, Pakistan. These were obtained using the RBT and C-ELISA in parallel as reported in Arif et al. (2019), in line with the recommendation on diagnostic test results in Arif et al. (2018a). The overall herd-level prevalence was 16.2% but this varied widely between districts (Table 1). The districts Jhelum and Pakpattan; Okara and Kasur; and Bhakkar, Thatta, and Badin, were found to have high (48%), medium (11%), and (effectively) no (<1%) disease prevalence respectively. This finding indicates that there is variability of Brucella in different geographical locations. It was found that the disease is present in the northern irrigated agro-ecological zone which is also an arid zone by agro-climatic classification. However, while the reasons behind the variation in prevalence are not known with certainty, it could be due to unfavorable climate conditions resulting in reduced survival and transmission of the organism, or it is also possible that the disease has not yet been introduced in those districts where it was not detected. However, to evaluate these possibilities, information on the movements of animals between districts is required as this may suggest geographic patterns of disease transmission. Although this is not possible in Pakistan currently, due to a lack of accurate record keeping that tracks animal movements between the districts, it is recommended that such capacity is prioritized in future development. Some reports from other countries identify an association between the disease and climate variables, for example, humidity, but in the current context/production system, further investigation is required, using finer-level climate data and larger numbers of sites, to explore this putative association.

Table 1: Herd-level prevalence estimates (%) of bovine brucellosis in seven districts of Pakistan. LPCI and UPCI are the lower and upper bounds of the 95% posterior credibility intervals. Values were obtained from Arif et al. (2018a).

Province	District	Prevalence	LPCI	UPCI
Punjab	Jhelum	45.1	31.7	58.8
	Kasur	4.8	1.0	12.8
	Okara	11.8	4.8	22.6
	Pakpattan	41.1	26.8	54.8
	Bhakkar	1.4	0.1	7.0
Sindh	Badin	1.6	0.1	7.9
	Thatta	1.1	0.0	6.0

6. KNOWLEDGE, ATTITUDES, PRACTICES (KAP) STUDY

The knowledge, attitudes, practices (KAP) study (Arif et al. 2017) assessed the extent of existing knowledge and understanding relating to brucellosis and investigated the occurrence of practices at the farm and household level that pose a risk for humans contracting brucellosis. The results of this study identified that, while smallholder dairy farmers had usually heard about animal brucellosis, there was little awareness regarding human brucellosis. In addition, almost all farmers reported that they performed at least one practice at both the farm and household level which poses a risk of Brucella transmission to other animals and humans. The results also revealed that the level of formal education of farmers is associated with their knowledge and understanding of the disease. The smallholder farmers with no formal education were less likely to be aware of the disease or perform good hygienic practices at their homes, compared with farmers with at least a middle level of formal education. This study was also carried out in seven districts and it was found that, although there was some variation, the prevalence of risky practices at both herd management and household level were high in all districts. Importantly this high level of risky practices occurred regardless of the disease prevalence, which was found to vary significantly between districts (Arif et al. 2019). This indicates that the presence of risky practices is likely to contribute to the spread of the disease where it is present. However, in the districts where the disease is not present, these practices still present a risk because if the disease is introduced in these regions it will spread quickly due favorable conditions and practices both in animals and humans.

This KAP study also comprehensively analyzed 'risk practice scores' (Farm cleaning risk score, Brucellosis herd transmission risk score, Household risk score) which are the total number of practices undertaken by farmers in each of their respective categories. These risky practice scores indicated that the knowledge of disease is an important predictor of the behavior as an increase in knowledge was associated with lower risk scores. None of the districts were risk-free in terms of practices undertaken by the majority of farmers and their families. Given the varied presence of Brucella between districts we can assert that there is no evidence of an association between risky behavior and presence or absence of Brucella at a district level, which is to be expected with a geographically-varied pathogen distribution. Therefore, if the disease is present (which is true for four of the seven districts investigated), a reduction in risky practices scores will eventually lead to a reduction in the prevalence of brucellosis. In addition, in areas where the disease is currently not present, a reduction in risky practices scores would be expected to reduce the chance of the disease spreading if it was introduced. Notably, the risky practices perceptions were also guided by cultural and religious beliefs which indicates that support to improve farmers' knowledge would not necessarily lead to practice change (Kansiime et al. 2014). The results of this research are useful to identify that not only will customization of the educational aspects of an intervention program be required, according to the risk profile of each region, but that customization without taking into account the cultural and religious sensitivities will result in limited change.

7. RISK FACTORS FOR BRUCELLOSIS

Based on the results reported by Arif et al. (2019), it was also found that last-trimester abortion, history of retained placenta, and the number of buffalo at farms were herd-level risk factors for the on-farm presence of brucellosis. The association with last-trimester abortion is in agreement with the biology of Brucella (McDermott et al. 1987) and similar findings have been reported in other studies (Boukary et al. 2013; Lindahl et al. 2014). The results of this study also suggest that larger numbers of buffalo on farms may be a risk factor for bovine brucellosis. However, this may be because there are a greater number of buffalo in the districts, as noted by Arif et al. (2019), with high disease prevalence and this association may be because the number of buffalo may be acting as a confounder or even an intervening variable, and consequently further investigations are required to determine the likely causal pathway, to adequately assess associations in future. The sampling approach used in this study resulted in a similar number of animals being sampled in each district, so this possible explanation could not be assessed from the data at hand. However, obtaining data on livestock density across geographical districts may help to resolve this issue. In conclusion, this research identified herd and animal risk factors associated with disease prevalence. This information can be used to design a targeted disease control program for the local field conditions of Pakistan, and the results can also be used to prioritize the districts for intervention, according to the disease status.

8. PARTICIPATORY EPIDEMIOLOGY: QUALITATIVE ON-FARM RESEARCH

To inform future interventions, the drivers, attitudes, and communication networks for improving the management of zoonotic diseases, with a focus on human brucellosis, among smallholder farmers in Pakistan was explored using a participatory epidemiology (PE) approach (Arif et al. 2018). The PE approach involves focus groups and individual in-depth interviews to understand how individuals and communities view health-related and other issues (Catley et al. 2012). Collectively, this work helps to understand brucellosis within the current smallholder settings and also provides direction to develop disease control programs for the smallholder production system which is the predominant system in Pakistan.

This study was carried out in the districts where the disease is present (Arif et al. 2019), i.e., Jhelum, Kasur, Okara and Pakpattan, and provides an insight into farmers' perception and knowledge. In particular, it shows that the farmers are not concerned about zoonotic disease, and this attitude is guided by either the economic cost or experience in terms of exposure to the disease or to any awareness program. Similarly, there was a marked difference or disconnect between farmers' perception of risky practices and the likelihood of performing these practices. Some of the practices are a part of the culture and traditional knowledge, for example, consumption of raw milk and its products, which makes practice change difficult, regardless of knowledge. These aspects need to be addressed by a culturally appropriate strategy when mechanisms for reduction are discussed and implemented. In addition, some risky practices are undertaken out of necessity as there are no viable alternative approaches, for example, animals are housed within homes as alternative space is not available for housing animals. These practices will be difficult to modify unless farmers can access support, and in some cases, additional resources (for example, land/space for housing). In addition, the analysis of communication networks in this study indicates that the farmers often use several unreliable or poorly informed sources either for information about or treatment of both animal and human health. There are several stakeholders that farmers should be sensitively counseled against using to seek information regarding disease prevention measures or treatment, for example senior farmers or religious leaders, unless it is known that they are well trained and knowledgeable in animal and human health aspects. The results revealed that farmers have more trust in senior farmers than veterinarians and that they would only contact a veterinarian or human health service providers in the case of an emergency. These findings indicate that there is a trust gap between farmers and health service providers (human and animal). Therefore, animal and human health providers should identify the trusted farmers within the village and work together to transfer important information about zoonotic diseases.

In conclusion, the results of this qualitative research, in conjunction with the KAP study (Arif et al. 2017), provide insight into farmer knowledge, attitudes, and practices that is imperative to guide a targeted educational intervention. We believe this intervention holds great importance in a smallholder context as testing and slaughtering of infected animals is not an economically and socially viable option in these settings. Typically, smallholders have between five to eight animals and their day-to-day livelihood depends on these animals. These communities are reported to have closer contact between animals and farming families (WHO 2006) than large and commercial farmers. Therefore, these smallholder farmers warrant a higher priority to receive health education regarding preventive measures for zoonotic disease, given that important zoonoses such as human brucellosis can be controlled very effectively by adopting risk-free practices with careful planning and implementation.

9. LIMITATIONS AND CONTEXTUALIZATION OF THE RESEARCH WORK

The findings of this study should be interpreted considering the context and the production system of Pakistan. Although we made every effort to reduce the biases, some limitations of the work are listed below.

Estimation of disease prevalence (Arif et al. 2017) was carried out on smallholder farms in seven districts of Pakistan, and so it follows that this will not be a perfect representation of the whole country. However, this is the first study carried out on smallholder farms in Pakistan with such a large number of samples and covering different agroecological zones. The findings indicate there is substantial variation in disease prevalence in the sampled districts which is very important information for designing a disease control program. This variation suggests there is no "one size fits all" or one intervention program that can be effective for the whole smallholder system across the country in terms of limiting the disease. However, despite this local variation, the results of disease burden might have more importance at the regional level, i.e. across the subcontinent, as these issues are equally applicable to other countries with smallholder production systems. Indeed, smallholder farms dominate the farming systems of most developing countries, many of which also have endemic brucellosis. Without having the disease burden information in smallholder settings, we cannot estimate the risk for human brucellosis.

Another potential limitation of this research could be the sampling approach for herd and animal-level prevalence estimation. It is understood that different sampling approaches are required for the selection of animals in small herds compared to large ones. For this study, we sampled a maximum of three animals per herd, but the herd size should not be overlooked when interpreting the results. The herds studied here are small: fewer than 10 animals in each and often only two or three. Indeed, just less than half of the farms sampled had herds comprised of three or fewer animals. So, overall, a sizeable proportion of animals were sampled from the farms, and it is considered that the sampling approach used here provides a good representation of mixed cattle and buffalo farms.

In this study, participants were selected from villages that were included as part of an Australian-funded project (ASLP Dairy Project) (Warriach et al. 2019). This could be another limiting factor as selected participants were smallholder farmers who were already directly or indirectly working with the project and had exposure to an extension program addressing the whole dairy farm system. Prior agreement to participate in this extension program may indicate that these farmers are somewhat more progressive, especially because the program involved engaging both men and women from farming families. In the same village, there is another group of farmers who have a traditional mindset and are less willing to participate in any developmental program. In some situations, such farmers also do not allow female farmers to participate in any program. Therefore, the results of this chapter should also be interpreted considering these factors. Nonetheless, we found a lack of knowledge and understanding regarding the disease and risky practices even in the group of smallholder farmers who have had exposure to some kind of extension program. Therefore, it is anticipated that the traditional group of smallholder farmers would have even less knowledge and understanding, and perhaps greater levels of risky practices. Further, this anticipated difference between the two groups of smallholder farmers within the same village might affect the way a future educational training program is implemented. We believe this is an important issue and it will be necessary to find a way to involve all farmers if a control program starts. This is beyond the scope of the current project but this gap needs to be considered for future work. Unless an intervention program can be implemented across the entire farming community in a village, this would leave a big proportion of the population at risk and the disease will persist, particularly in villages that practice common grazing because of the greater risk of the disease spreading in this scenario.

Future work also needs to consider the concept of what should be considered a herd, as this research shows that there are several farmers who send their animals for common grazing with other animals of the village. This would suggest that in those villages, the whole village may be considered a herd as animals are mixing. Further studies to understand the nature of common grazing and disease transmission across village livestock may be valuable to identify the likely effect of this mixing pattern on disease transmission. This may indicate if villages with common grazing need a different intervention program.

10. OUTLINE OF ISSUES FOR AN INTERVENTION PROGRAM

This research shows the need for a targeted intervention program in Pakistan, both to guide an educational program and for bovine brucellosis screening and control programs. The intervention program must provide a longer-term solution rather than a 'quick fix' to the problem. No single solution can solve this problem, and a holistic approach is required which includes realistic and achievable objectives. It must be very broadly based and take into consideration societal and community issues, educational aspects, as well as the epidemiology of the zoonotic disease. Below is a brief outline of what needs to be considered, based on the results of this research, if we would proceed to start an intervention program.

For an effective intervention program, categorization of the districts into low or high prevalence regions is imperative, to implement effective targeted intervention. This essentially represents a 'risk-based intervention' program. Categorization of districts can be done by carrying out a small cross-sectional study in each region to estimate seroprevalence using the approach and tests described by Arif et al. (2017), Arif et al. (2019). For example, from the current study, a district with high disease prevalence (Jhelum) and one with low prevalence (Bhakkar) would be selected in the initial phase of an intervention program. If the prevalence in an intervention area is high, then we may adopt an intense educational intervention via farmer discussion groups using trusted individuals. However, for areas where the disease is absent or has very low prevalence, then we could adopt a less intensive mass communication program to convey health information to the farming communities.

The development of training material on disease preventive measures with support from social scientists who have extensive knowledge of the culture and religion within each region would be beneficial. Ideally, this training material would include fact sheets and short videos in the local language on different topics. Highlighting certain disease scenarios or short case studies of the risky practice both at the farm and household level would allow farmers to personally identify with these issues and allow interpretation by educated and non-educated members of the community. Educational awareness should also be provided through trusted sources of animal and human health providers as highlighted in the PE study (Arif et al. 2018). Educational sessions should be carried out in the form of focus groups both for men and women, conducted separately because of cultural sensitivities and different risk perceptions. Furthermore, this educational intervention should be carried out in districts with both high and low disease prevalence (for prevention of the spread of disease in the future) but if fewer resources are available then priority will be given to districts with high disease prevalence.

In addition, if there are sufficient resources, this would allow an intervention team to also quality vaccinate the animals in high prevalence areas. However, this would require prior training of veterinary assistants about vaccination handling since the Brucella vaccine is live and itself carries a risk for disease transmission if it is not handled properly. Both disease screening and vaccination can significantly reduce the prevalence of the disease in animals which will also result in a reduction in the risk of human brucellosis and increase animal production. While vaccination is often used as an important step in disease control, within a smallholder context such as that studied here, likely, this will not represent a valid option. The cost of vaccination, given the lack of local production, along with the difficulty in handling and the lack of appropriately trained administrators, are all rate-limiting issues at this stage. As such, awareness of disease and behavior change are more appropriate interventions in this environment in the short term.

To enhance the effectiveness of an intervention program, a phased introduction is recommended. For this, at least one village should be selected as an intervention village, and a corresponding number of villages without intervention. An impact assessment of the program can be performed by carrying out a small KAP study, perhaps supported by focus group interviews. This will be helpful to assess any improvement in the practices and also to make any modifications if required. This model can be replicated or rolled out to other villages or districts, but again its impacts need to be assessed.

To run a control program there will be an absolute need to involve government livestock and human health departments 'on the ground' and other stakeholders. In Pakistan, zoonotic diseases are currently not addressed by either of these government agencies, however, a synergistic One Health approach is required by both departments to guarantee both dimensions are covered in an integrated and cooperative way. The control program would equip the field staff of both departments to disseminate the program at a 'grassroots' level.

Before implementing a control program there is also a need to conduct a cost-benefit analysis. For example, a cost-benefit analysis was recently conducted in India to assess the viability of a brucellosis intervention program for cattle and buffalo (Singh et al. 2018). Such a program can be more cost-effective if it is rolled out with other intervention programs, for example, a tuberculosis control program. Also, a risk assessment study could be performed to assess if there is any risk involved in implementing such an intervention program. Critically, this evaluation (costs, benefits, risks) must be broadly based, with input from the government stakeholders, but also involve local rural communities, as without their commitment, it is difficult to consider that a program could be successful.

11. CONCLUSION

The findings outlined in this chapter can be explained in the form of a complex network involving the interactions between farmers, livestock, and Brucella organisms, together with the environments they all operate in. Addressing this complex network has required the use of a range of epidemiological tools, involving both quantitative and qualitative approaches, to evaluate the disease burden over seven districts of Pakistan and to identify the best combination of diagnostic procedures to be used in field conditions in this country (RBT and C-ELISA in parallel combination). Using these methods, it was found that Brucella infection is present in cattle and buffalo in four out of the seven districts studied, some with high disease prevalence, and this can constitute a substantial public health risk for rural smallholder communities as well as resulting in production losses for this system. In addition, a range of practices were identified that pose a risk of brucellosis, not only to livestock but also to humans, given the intimate contact between livestock and their owners in rural communities. Further insights about brucellosis and other zoonotic diseases in terms of farmers' understanding, risk perception, and sources of information were obtained from a series of in-depth farmer interviews and textual analyses, in particular exploring gender differences. These findings work together to increase our understanding of brucellosis in the smallholder systems of Pakistan, particularly through a 'One Health' perspective. This information provides the foundations on which to build an intervention program to reduce the impact of this disease on animals and humans. In conclusion, the findings and recommendations presented in this chapter can help to guide future intervention programs that will result in marked added value to the smallholder communities in Pakistan.

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